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156

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157

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158

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159

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160

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162

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163

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164

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166

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168

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169

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170

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172

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174

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176

ANNTANAGTTTGAGGGAAAGGAGGTAAGAATTGACACAAATAAGTAATGTCATGTGCCTAAAATGACTGAAGATTCAGTAAAGA
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178

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180

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181

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182

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184

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186

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187

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188

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190

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192

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194

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196

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198

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200

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201

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202

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204

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205

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206

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207

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208

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209

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210

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212

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214

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216

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217

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218

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219

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220

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221

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222

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223

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224

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225

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226

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227

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228

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229

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230

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231

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232

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233

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234

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235

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236

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237

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238

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340

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239

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240

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241

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242

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243

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244

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246

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247

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248

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249

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250

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251

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253

MGKVKVGVNGFGRIGRLVTRAAFNSGKVDIVAINDPFIDLNYMVYMFQYDSTHGKFHGTVKAENGKLVINGNPITIFQERDPSK
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254

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255

MSLSNKLTLDKLDVKGKRVVMRVDFNVPMKNNQITNNQRIKAAVPSIKFCLDNGAKSVVLMSHLGRPDGVPMPDKYSLEPVAVE
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256

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257

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258

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259

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260

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261

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262

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263

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264

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265

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266

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267

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268

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269

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270

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271

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272

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273

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274

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275

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276

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277

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278

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279

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280

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282

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283

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284

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285

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286

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287

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288

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289

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290

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291

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292

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293

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294

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295

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296

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360

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297

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298

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299

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300

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301

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302

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303

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304

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305

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306

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307

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308

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309

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310

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311

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312

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313

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313

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314

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315

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316

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317

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318

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319

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320

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321

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322

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323

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324

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325

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326

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327

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328

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329

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330

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331

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332

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333

MALKERIGWRYSLLFVGLLQLNIVVFGALLRPIIIRGPASPKIVIQENRKEAQYMLENEKTRTSIDSIDSGVELTTSPKNVPTH
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334

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335

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336

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337

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338

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339

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FLDR

340

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341

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342

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343

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344

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345

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346

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347

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348

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349

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350

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351

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352

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353

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354

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355

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356

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357

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358

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359

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360

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361

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362

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363

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364

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365

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366

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367

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368

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369

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370

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371

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372

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373

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374

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375

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376

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377

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378

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379

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380

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381

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382

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383

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384

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385

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386

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387

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388

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389

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390

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391

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392

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394

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395

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396

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397

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398

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400

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401

400

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402

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403

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404

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401

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405

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407

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408

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409

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410

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411

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412

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413

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414

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415

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416

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417

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418

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419

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420

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421

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422

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423

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424

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425

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426

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427

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428

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429

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430

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431

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432

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433

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434

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435

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436

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437

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438

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439

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440

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441

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442

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443

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444

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446

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447

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448

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449

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450

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451

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452

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454

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455

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456

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457

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458

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459

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460

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461

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462

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463

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464

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465

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466

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467

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468

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469

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470

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471

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472

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473

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474

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475

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476

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GGAAACTGATTAATAGAGATAGCAAGGGATAATTAAATAAATATTCCCTATGTAGCAACAGTGGTTAGATGATCTTTGTCTGAA
TGTAATAAAACTTTGAATAGTTTTAGTGTGTCCTTAAAGCCAAGTATATGCTTTAACATCAAATGGAAGTCAAATTCCTAATGC
ATAGATAGAGAGAGCTAAACTGTGTAATTTAATGGTATCTTCCTTGCTGGATGTGGCAGAATCCACACCAGCTTATCAACCAAC
ACAGCTAATTTTAGAATAGGTCCTTTATCTTTCCATATGGCACACGTAAGAAAGTGTTTTTCTACTATTAATATTAAATTAAAA
CCTTTACTTTTGTATAATAAATTAAAACTCAGAATAAACCTGTGACCACGT

477

MAENGDNEKMAALEAKICHQIEYYFGDFNLPRDKFLKEQIKLDEGWVPLEIMIKFNRLNRLTTDFNVIVEALSKSKAELMEISE
DKTKIRRSPSKPLPEVTDEYKNDVKNRSVYIKGFPTDATLDDIKEWLEDKGQVLNIQMRRTLHKAFKGSIFVVFDSIESAKKFV
ETPGQKYKETDLLILFKDDYFAKKNEERKQNKVEAKLRAKQEQEAKQKLEEDAEMKSLEEKIGCLLKFSGDLDDQTCREDLHIL
FSNHGEIKWIDFVRGAKEGIILFKEKAKEALGKAKDANNGNLQLRNKEVTWEVLEGEVEKEALKKIIEDQQESLNKWKSKGRRF
KGKGKGNKAAQPGSGKGKVQFQGKKTKFASDDEHDEHDENGATGPVKRAREETDKEEPASKQQKTENGAGDQ

478

GGAGTCGTTGTTGTTGCTGTTTGTGAGCCTGTGCGGCGGCTTCTGTGGGCCGGAACCTTAAAGATAGCCGCAATGGCTGAAAAT
GGTGATAATGAAAAGATGGCTGCCCTGGAGGCCAAAATCTGTCATCAAATTGAGTATTATTTTGGCGACTTCAATTTGCCACGG
GACAAGTTTCTAAAGGAACAGATAAAACTGGATGAAGGCTGGGTACCTTTGGAGATAATGATAAAATTCAACAGGTTGAACCGT
CTAACAACAGACTTTAATGTAATTGTGGAAGCATTGAGCAAATCCAAGGCAGAACTCATGGAAATCAGTGAAGATAAAACTAAA
ATCAGAAGGTCTCCAAGCAAACCCCTACCTGAAGTGACTGATGAGTATAAAAATGATGTAAAAAACAGATCTGTTTATATTAAA
GGCTTCCCAACTGATGCAACTCTTGATGACATAAAAGAATGGTTAGAAGATAAAGGTCAAGTACTAAATATTCAGATGAGAAGA
ACATTGCATAAAGCATTTAAGGGATCAATTTTTGTTGTGTTTGATAGCATTGAATCTGCTAAGAAATTTGTAGAGACCCCTGGC
CAGAAGTACAAAGAAACAGACCTGCTAATACTTTTCAAGGACGATTACTTTGCCAAAAAAAAATGAAGAAAGAAAACAAAATAAA
GTGGAAGCTAAATTAAGAGCTAAACAGGAGCAAGAAGCAAAACAAAAGTTAGAAGAAGATGCTGAAATGAAATCTCTAGAAGAA
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GGTGAAATAAAATGGATAGACTTCGTCAGAGGAGCAAAAGAGGGGATAATTCTATTTAAAGAAAAAGCCAAGGAAGCATTGGGT
AAAGCCAAAGATGCAAATAATGGTAACCTACAATTAAGGAACAAAGAAGTGACTTGGGAAGTACTAGAAGGAGAGGTGGAAAAA
GAAGCACTGAAGAAAATAATAGAAGACCAACAAGAATCCCTAAACAAATGGAAGTCAAAAGGTCGTAGATTTAAAGGAAAAGGA
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GAACATGATGAACATGATGAAAATGGTGCAACTGGACCTGTGAAAAGAGCAAGAGAAGAAACAGACAAAGAAGAACCTGCATCC
AAACAACAGAAAACAGAAAATGGTGCTGGAGACCAGTAGTTTAGTAAACCAATTTTTTATTCATTTTAAATAGGTTTTAAACGA
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GTTTAACTTGTCTTTTTGTTATGCAAATGAGATTTCTTTGAATGTATTGTTCTGTTTGTGTTATTTCAGATGATTCAAATATCA
AAAGGAAGATTCTTCCATTAAATTGCCTTTGTAATATGAGAATGTATTAGTACAAACTAACTAATAAAATATATACTATATGAA
AAGAGCAAAAAAAAAAAAAAAAA

479

MLKLTPLPSKMKVSAALLCLLLMAATFSPQGLAQPDSVSIPITCCFNVINRKIPIQRLESYTRITNIQCPKEAVIFKTQRGKEV
CADPKERWVRDSMKHLDQIFQNLKP

480

ATGCTGAAGCTCACACCCTTGCCCTCCAAGATGAAGGTTTCTGCAGCGCTTCTGTGCCTGCTGCTCATGGCAGCCACTTTCAGC
CCTCAGGGACTTGCTCAGCCAGATTCAGTTTCCATTCCAATCACCTGCTGCTTTAACGTGATCAATAGGAAAATTCCTATCCAG
AGGCTGGAGAGCTACACAAGAATCACCAACATCCAATGTCCCAAGGAAGCTGTGATCTTCAAGACCCAACGGGGCAAGGAGGTC
TGTGCTGACCCCAAGGAGAGATGGGTCAGGGATTCCATGAAGCATCTGGACCAAATATTTCAAAATCTGAAGCCATGA

481

MARATLSAAPSNPRLLRVALLLLLLVAASRRAAGAPLATELRCQCLQTLQGIHLKNIQSVKVKSPGPHCAQTEVIATLKNGQKA
CLNPASPMVKKIIEKMLKNGKSN

482

GACAGAGCCCGGGCCACGGAGCTCCTTGCCAGCTCTCCTCCTCGCACAGCCGCTCGAACCGCCTGCTGAGCCCCATGGCCCGCG
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GTGATGACATATCACATGTCAGCCACTGTGATAGAGGCTGAGGAATCCAAGAAAATGGCCAGTAAGATCAATGTGACGGCAGGG
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TTTCTCATGTTGAAGCTTTAAGAACTAAAATGTTCTAAATATCCCTTGGCATTTTATGTCTTTCTTGTAAGATACTGCCTTGTT
TAATGTTAATTATGCAGTGTTTCCCTCTGTGTTAGAGCAGAGAGGTTTCGATATTTATTGATGTTTTCACAAAGAACAGGAAAA
TAAAATATTTAAAAATAT

483

MKLVRFLMKLSHETVTIELKNGTQVHGTITGVDVSMNTHLKAVKMTLKNREPVQLETLSIRGNNIRYFILPDSLPLDTLLVDVE
PKVKSKKREAVAGRGRGRGRGRGRGRGRGGPRR

484

GAATTCCCCCCCCCCCCCCAGTGCTCCGCGCGCTCTTGACGTCCGGAGCCCCTGGAGTAGGCGCTTCCGGCCATTCATACTGCA
GTCGGTCAGTGTTCGGTTGAAGGATTCTGTGTGCTGTCGGACCCAGAGGGTGACGGCGCCGCTAGGATGAAGCTCGTGAGATTT
TTGATGAAATTGAGTCATGAAACTGTAACCATTGAATTGAAGAACGGAACACAGGTCCATGGAACAATCACAGGTGTGGATGTC
AGCATGAATACACATCTTAAAGCTGTGAAAATGACCCTGAAGAACAGAGAACCTGTACAGCTGGAAACGCTGAGTATTCGAGGA
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CGATAATGTCTCTCAAGATTTCAAAGTCATATGAGATTTGGGATATTTTTTGTACAGGTTGTGTTTGTTTATGTCAGTTTTTAA
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ATGATGAATAAGGTTAAAATAAAAGCCTTAGACAAATTAAATTTGGCAGAGTTTAATTGAGCAAAGGACAATTCACAAATCAGG
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TGGTATTTCGGAAACTAAAGTCCTTATGGGATGGGGTCTAGAATTGATTCTCCTTTCCTGAGTTTTACTCCACGGAGTCTTAGG
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TTTAATCAGTTCTTAATAGGATATAGTTTTATGTTTTCCAAGTTATAACTTGGAGTTAATGGTCACTAGATTATCAGTTATGAG
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ACCTACTTTATTTGACAGCAAAAAAAAAAAGGAATTC

485

MARAALSAAPSNPRLLRVALLLLLLVAAGRRAAGASVATELRCQCLQTLQGIHPKNIQSVNVKSPGPHCAQTEVIATLKNGRKA
CLNPASPIVKKIIEKMLNSDKSN

486

CACAGAGCCCGGGCCGCAGGCACCTCCTCGCCAGCTCTTCCGCTCCTCTCACAGCCGCCAGACCCGCCTGCTGAGCCCCATGGC
CCGCGCTGCTCTCTCCGCCGCCCCCAGCAATCCCCGGCTCCTGCGAGTGGCACTGCTGCTCCTGCTCCTGGTAGCCGCTGGCCG
GCGCGCAGCAGGAGCGTCCGTGGCCACTGAACTGCGCTGCCAGTGCTTGCAGACCCTGCAGGGAATTCACCCCAAGAACATCCA
AAGTGTGAACGTGAAGTCCCCCGGACCCCACTGCGCCCAAACCGAAGTCATAGCCACACTCAAGAATGGGCGGAAAGCTTGCCT
CAATCCTGCATCCCCCATAGTTAAGAAAATCATCGAAAAGATGCTGAACAGTGACAAATCCAACTGACCAGAAGGGAGGAGGAA
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GAATGTATGTGCACATCTGTTTTGTAACTGTTTAGATGAATGTCAGTTGTTATTTATTGAAATGATTTCACAGTGTGTGGTCAA
CATTTCTCATGTTGAAACTTTAAGAACTAAAATGTTCTAAATATCCCTTGGACATTTTATGTCTTTCTTGTAAGGCATACTGCC
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AGCACTTATAG

487

MIFPWKCQSTQRDLWNIFKLWGWTMLCCDFLAHHGTDCWTYHYSEKPMNWQRARRFCRDNYTDLVAIQNKAEIEYLEKTLPFSR
SYYWIGIRKIGGIWTWVGTNKSLTEEAENWGDGEPNNKKNKEDCVEIYIKRNKDAGKWNDDACHKLKAALCYTASCQPWSCSGH
GECVEIINNYTCNCDVGYYGPQCQFVIQCEPLEAPELGTMDCTHPLGNFSFSSQCAFSCSEGTNLTGIEETTCGPFGNWSSPEP
TCQVIQCEPLSAPDLGIMNCSHPLASFSFTSACTFICSEGTELIGKKKTICESSGIWSNPSPICQKLDKSFSMIKEGDYNPLFI
PVAVMVTAFSGLAFIIWLARRLKKGKKSKRSMNDPY

488

CTCCCTTTGGGCAAGGACCTGAGACCCTTGTGCTAAGTCAAGAGGCTCAATGGGCTGCAGAAGAACTAGAGAAGGACCAAGCAA
AGCCATGATATTTCCATGGAAATGTCAGAGCACCCAGAGGGACTTATGGAACATCTTCAAGTTGTGGGGGTGGACAATGCTCTG
TTGTGATTTCCTGGCACATCATGGAACCGACTGCTGGACTTACCATTATTCTGAAAAACCCATGAACTGGCAAAGGGCTAGAAG
ATTCTGCCGAGACAATTACACAGATTTAGTTGCCATACAAAACAAGGCGGAAATTGAGTATCTGGAGAAGACTCTGCCTTTCAG
TCGTTCTTACTACTGGATAGGAATCCGGAAGATAGGAGGAATATGGACGTGGGTGGGAACCAACAAATCTCTTACTGAAGAAGC
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CAGCTTTACCTCTGCATGTACCTTCATCTGCTCAGAAGGAACTGAGTTAATTGGGAAGAAGAAAACCATTTGTGAATCATCTGG
AATCTGGTCAAATCCTAGTCCAATATGTCAAAAATTGGACAAAAGTTTCTCAATGATTAAGGAGGGTGATTATAACCCCCTCTT
CATTCCAGTGGCAGTCATGGTTACTGCATTCTCTGGGTTGGCATTTATCATTTGGCTGGCAAGGAGATTAAAAAAAGGCAAGAA
ATCCAAGAGAAGTATGAATGACCCATATTAAATCGCCCTTGGTGAAAGAAAATTCTTGGAATACTAAAAATCATGAGATCCTTT
AAATCCTTCCATGAAACGTTTTGTGTGGTGGCACCTCCTACGTCAAACATGAAGTGTGTTTCCTTCAGTGCATCTGGGAAGATT
TCTACCTGACCAACAGTTCCTTCAGCTTCCATTTCGCCCCTCATTTATCCCTCAACCCCCAGCCCACAGGTGTTTATACAGCTC
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CTTTCTTGACTCTTGTTTTCAGTTTCAATTCAGTGCTGTACTTGATGACAGACACTTCTAAATGAAGTGCAAATTTGATACATA
TGTGAATATGGACTCAGTTTTCTTGCAGATCAAATTTCACGTCGTCTTCTGTATACTGTGGAGGTACACTCTTATAGAAAGTTC
AAAAAGTCTACGCTCTCCTTTCTTTCTAACTCCAGTGAAGTAATGGGGTCCTGCTCAAGTTGAAAGAGTCCTATTTGCACTGTA
GCCTCGCCGTCTGTGAATTGGACCATCCTATTTAACTGGCTTCAGCCTCCCCACCTTCTTCAGCCACCTCTCTTTTTCAGTTGG
CTGACTTCCACACCTAGCATCTCATGAGTGCCAAGCAAAAGGAGAGAAGAGAGAAATAGCCTGCGCTGTTTTTTAGTTTGGGGG
TTTTGCTGTTTCCTTTTATGAGACCCATTCCTATTTCTTATAGTCAATGTTTCTTTTATCACGATATTATTAGTAAGAAAACAT
CACTGAAATGCTAGCTGCAAGTGACATCTCTTTGATGTCATATGGAAGAGTTAAAACAGGTGGAGAAATTCCTTGATTCACAAT
GAAATGCTCTCCTTTCCCCTGCCCCCAGACCTTTTATCCACTTACCTAGATTCTACATATTCTTTAAATTTCATCTCAGGCCTC
CCTCAACCCCACCACTTCTTTTATAACTAGTCCTTTACTAATCCAACCCATGATGAGCTCCTCTTCCTGGCTTCTTACTGAAAG
GTTACCCTGTAACATGCAATTTTGCATTTGAATAAAGCCTGCTTTTTTAAGTGTTAA

CLAIMS

1. A method for the identification of a gene that is implicated in a specific disease or physiological condition, said method comprising the steps of:

a) comparing:

i) the transcriptome or proteome of a first specialised cell type that is implicated in the disease or condition under first and second experimental conditions; with

ii) the transcriptome or proteome of a second specialised cell type under said first and said second experimental conditions; and

b) identifying as a gene implicated in the disease or physiological condition, a gene that is differentially regulated in the two specialised cell types under the first and second experimental conditions.

2. A method according to claim 1, wherein said specialised cell types are selected from the group consisting of cardiomyocytes, endothelial cells, sensory neurons, motor neurons, CNS neurons, astrocytes, glial cells, schwann cells, mast cells, eosinophils, smooth muscle cells, skeletal muscle cells, pericytes, lymphocytes, tumor cells, monocytes, macrophages, foamy macrophages, granulocytes, synovial cells / synovial fibroblasts and epithelial cells.

3. A method according to claim 1 or claim 2, wherein said first and second experimental conditions differ in respect of the cellular microenvironment, or in respect of exposure to hormones, growth factors, cytokines, chemokines, inflammatory agents, toxins, metabolites, pH, pharmaceutical agents, hypoxia, anoxia, ischemia, imbalance of any plasma-borne nutrient, osmotic stress, temperature, mechanical stress, irradiation, cell-extracellular matrix interactions, cell-cell interactions, accumulations of foreign or pathological extracellular components, intracellular and extracellular pathogens, or a genetic perturbation.

4. A method according to any one of the preceding claims, wherein the first experimental conditions and second experimental conditions differ in that under the second experimental conditions, the cells are exposed to a physiological stimulus.

5. A method according to claim 4, wherein the physiological stimulus is a physiological, mechanical, temperature, chemical, toxic or pharmaceutical stress.

6. A method according to claim 5, wherein said physiological stress is hypoxia.

7. A method according to any one of the preceding claims, wherein said first and second experimental conditions are different genetic conditions.

8. A method according to claim 7, wherein said second experimental conditions differ from said first experimental conditions in that the expression of a genetic element is expressed at a different level in said second experimental conditions relative to the level of expression of the genetic element in said first experimental conditions.

9. A method according to claim 8, wherein said genetic element is heterologous to the specialized cell type.

10. A method according to any one of the preceding claims, wherein the transcriptomes of the specialized cell types are compared by a technique involving hybridization to a nucleic acid array, subtractive mRNA hybridisation, the serial analysis of gene expression (SAGE); the selective amplification via biotin- and restriction-mediated enrichment (SABRE); differential display; representational difference analysis (RDA); differential screening of cDNA libraries; Northern blotting; an RNAse protection assay; an S1-nuclease protection assays; RT-PCR; real time RT-PCR (Taq-man); EST sequencing; massively parallel signature sequencing (MPSS); or sequencing by hybridisation (SBH).

11. A method according to claim 10, wherein the transcriptomes are compared by hybridization to a nucleic acid array.

12. A substantially purified polypeptide, encoded by a gene implicated in a specific disease or physiological condition by a method according to any one of the preceding claims.

13. A substantially purified polypeptide, which polypeptide:

i) comprises the amino acid sequence as recited in any one of SEQ ID Nos: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 63, 67, 69, 73, 75, 77, 85, 87, 89, 91, 93, 95, 99, 103, 113, 115, 119, 121, 129, 131, 133, 137, 139, 141, 145, 151, 153, 157, 159, 163, 169, 181, 187, 201, 205, 207 and 209;

ii) has an amino acid sequence encoded by a nucleic acid sequence recited in any one of SEQ ID Nos: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 92a, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200,

202, 204, 206, 208, 210, 212, 214 and 216, or has an amino acid sequence encoded by a gene identified from an EST recited in any one of these SEQ ID Nos;

iii) is a fragment of a polypeptide according to i) or ii), provided that said fragment retains a biological activity possessed by the full length polypeptide of i) or ii), or has an antigenic determinant in common with the polypeptide of i) or ii); or

iv) is a functional equivalent of a polypeptide of i), ii) or (iii).

14. A polypeptide according to claim 13, wherein said biological activity is a hypoxia-regulated activity.

15. A polypeptide according to claim 14, wherein the expression of the polypeptide is hypoxia-induced.

16. A polypeptide according to claim 15, which polypeptide:

i) comprises the amino acid sequence as recited in any one of SEQ ID Nos.: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 63, 67, 69, 73, 75, 77, 85, 87, 89, 91, 93, 95, 99, 103, 113, 115, 119, 121, 129, 131, 133, 137, 139 and 141;

ii) has an amino acid sequence encoded by a nucleic acid sequence recited in any one of SEQ ID Nos.: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 92a, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142 and 144, or is encoded by a gene identified from an EST recited in any one of these SEQ ID Nos.;

iii) is a fragment of a polypeptide according to i) or ii), provided that said fragment retains a biological activity possessed by the full length polypeptide of i) or ii), or has an antigenic determinant in common with the polypeptide of i) or ii); or

iv) is a functional equivalent of a polypeptide of i), ii) or (iii).

17. A polypeptide according to claim 14, wherein the expression of the polypeptide is hypoxia-repressed.

18. A polypeptide according to claim 17, which polypeptide:

i) comprises the amino acid sequence as recited in any one of SEQ ID Nos.: 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 145, 151, 153, 157, 159, 163, 169, 181, 187, 201, 205, 207 and 209;

ii) has an amino acid sequence encoded by a nucleic acid sequence recited in any one of SEQ ID Nos.: 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192,

194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214 and 216, or is encoded by a gene identified from an EST recited in any one of these SEQ ID Nos.;

iii) is a fragment of a polypeptide according to i) or ii), provided that said fragment retains a biological activity possessed by the full length polypeptide of i) or ii), or has an antigenic determinant in common with the polypeptide of i) or ii); or

iv) is a functional equivalent of a polypeptide of i), ii) or (iii).

19. A polypeptide which is a functional equivalent according to part iv) of any one of claims 13-18, is homologous to the amino acid sequence as recited in any one of SEQ ID Nos: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 63, 67, 69, 73, 75, 77, 85, 87, 89, 91, 93, 95, 99, 103, 113, 115, 119, 121, 129, 131, 133, 137, 139, 141, 145, 151, 153, 157, 159, 163, 169, 181, 187, 201, 205, 207 and 209 or is homologous to the amino acid sequence encoded by a nucleic acid as recited in any one of SEQ ID Nos: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 92a, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214 and 216, and has equivalent biological activity to that possessed by the full length polypeptide of i) or ii).

20. A fragment or functional equivalent according to any one of claims 13-19, which has greater than 50% sequence identity with the amino acid sequence as recited in any one of SEQ ID Nos: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 63, 67, 69, 73, 75, 77, 85, 87, 89, 91, 93, 95, 99, 103, 113, 115, 119, 121, 129, 131, 133, 137, 139, 141, 145, 151, 153, 157, 159, 163, 169, 181, 187, 201, 205, 207 and 209 or with the amino acid sequence that is encoded by a nucleic acid as recited in any one of SEQ ID Nos: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 92a, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214 and 216, or with fragments thereof, preferably greater than 60%, 70%, 80%, 90%, 95%, 98% or 99% sequence identity.

21. A fragment as recited in any one of claims 13-20 having an antigenic determinant in common with a polypeptide according to part i) of any one of claims 13-18, which consists of 7 or more (for example,

8, 10, 12, 14, 16, 18, 20 or more) amino acid residues from the amino acid sequence as recited in any one of SEQ ID Nos: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 63, 67, 69, 73, 75, 77, 85, 87, 89, 91, 93, 95, 99, 103, 113, 115, 119, 121, 129, 131, 133, 137, 139, 141, 145, 151, 153, 157, 159, 163, 169, 181, 187, 201, 205, 207 and 209 or the amino acid sequence encoded by a nucleic acid as recited in any one of SEQ ID Nos: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 92a, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214 and 216.

22. A purified and isolated nucleic acid molecule that encodes a polypeptide according to any one of claims 13-21.

23. A purified nucleic acid molecule according to claim 22, which consists of the nucleic acid sequence as recited in any one of SEQ ID Nos.: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 92a, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214 and 216, or is a redundant equivalent or fragment thereof.

24. A purified nucleic acid molecule which hydridizes under high stringency conditions with a nucleic acid molecule according to claim 22 or claim 23.

25. A vector comprising a nucleic acid molecule as recited in any one of claims 22-24.

26. A delivery vehicle comprising a nucleic acid according to any one of claims 22-24 or a vector according to claim 25.

27. A host cell transformed with a vector according to claim 25.

28. An antagonist ligand which binds specifically to a polypeptide according to any one of claims 13-21, preferably a ligand which inhibits the hypoxia-induced activity of said polypeptide.

29. An agonist ligand which binds specifically to a polypeptide according to any one of claims 13-21, preferably a ligand which augments or potentiates a hypoxia-induced activity of said polypeptide.

30. A ligand according to claim 28 or claim 29, which is an antibody.

31. A ligand according to claim 28 or claim 29, which is a peptide, a peptidomimetic, or a drug molecule, such as a small natural or synthetic organic molecule of up to 2000Da, preferably 800Da or less.

32. A polypeptide according to any one of claims 13-21, a nucleic acid molecule according to any one of claims 22-24, a vector according to claim 25 or a ligand according to claim 30 or 31, for use in therapy or diagnosis of disease.

33. A polypeptide, nucleic acid molecule, vector or ligand as recited in claim 32, wherein said disease is a hypoxia-regulated condition.

34. A polypeptide, nucleic acid molecule, vector or ligand as recited in claim 33, wherein said hypoxia-regulated condition is tumourigenesis, angiogenesis, apoptosis, inflammation, erythropoiesis, the biological response to hypoxia conditions (including processes such as glycolysis, gluconeogenesis, glucose transportation, catecholamine synthesis, iron transport or nitric oxide synthesis).

35. A substantially purified polypeptide, which polypeptide:

i) comprises the amino acid sequence as recited in any one of SEQ ID Nos: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 63, 67, 69, 73, 75, 77, 85, 87, 89, 91, 93, 95, 99, 103, 113, 115, 119, 121, 129, 131, 133, 137, 139, 141, 145, 151, 153, 157, 159, 163, 169, 181, 187, 201, 205, 207 and 209 or SEQ ID Nos.: 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391, 393, 395, 397, 399, 401, 403, 405, 407, 409, 411, 413, 415, 417, 419, 421, 423, 425, 427, 429, 431, 433, 435, 437, 439, 441, 443, 445, 447, 449, 451, 453, 455, 457, 459, 461, 463, 465, 467, 469, 471, 473, 475, 477, 479, 481, 483, 485 and 487;

ii) has an amino acid sequence encoded by a nucleic acid sequence recited in any one of SEQ ID Nos: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 92a, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200,

202, 204, 206, 208, 210, 212, 214 and 216, or has an amino acid sequence encoded by a gene identified from an EST recited in any one of these SEQ ID Nos;

iii) is a fragment of a polypeptide according to i) or ii), provided that said fragment retains a biological activity possessed by the full length polypeptide of i) or ii), or has an antigenic determinant in common with the polypeptide of i) or ii); or

iv) is a functional equivalent of a polypeptide of i), ii) or (iii).

for use in the diagnosis or therapy of the disease or abnormal physiological condition that is affected by hypoxia, such as cancer, ischaemic conditions, reperfusion injury, retinopathy, neonatal stress, preeclapmsia, atherosclerosis, inflammatory conditions, wound healing, tumourigenesis, angiogenesis, apoptosis, inflammation, erythropoiesis, hair loss, or the biological response to hypoxia conditions, including processes such as glycolysis, gluconeogenesis, glucose transportation, catecholamine synthesis, iron transport and nitric oxide synthesis.

36. A purified and isolated nucleic acid molecule that encodes a polypeptide as recited in claim 35, for use in the diagnosis or therapy of for use in the diagnosis or therapy of a disease or abnormal physiological condition that is affected by hypoxia, such as cancer, ischaemic conditions, reperfusion injury, retinopathy, neonatal stress, preeclapmsia, atherosclerosis, inflammatory conditions, wound healing, tumourigenesis, angiogenesis, apoptosis, inflammation, erythropoiesis or hair loss.

37. A purified nucleic acid molecule as recited in claim 36, which consists of the nucleic acid sequence as recited in any one of SEQ ID Nos.: 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392, 394, 396, 398, 400, 402, 404, 406, 408, 410, 412, 414, 416, 418, 420, 422, 424, 426, 428, 430, 432, 434, 436, 438, 440, 442, 444, 446, 448, 450, 452, 454, 456, 458, 460, 462, 464, 466, 468, 470, 472, 474, 476, 478, 480, 482, 484, 486 and 488, or which is a redundant equivalent or fragment thereof, for use in the diagnosis or therapy of a disease or abnormal physiological condition that is affected by hypoxia, such as cancer, ischaemic conditions, reperfusion injury, retinopathy, neonatal stress, preeclapmsia, atherosclerosis, inflammatory conditions, wound healing, tumourigenesis, angiogenesis, apoptosis, inflammation, erythropoiesis or hair loss.

38. A purified nucleic acid molecule which hydridizes under high stringency conditions with a nucleic acid molecule as recited in claim 36 or claim 37, for use in the diagnosis or therapy of a disease or

abnormal physiological condition that is affected by hypoxia, such as cancer, ischaemic conditions, reperfusion injury, retinopathy, neonatal stress, preeclapmsia, atherosclerosis, inflammatory conditions, wound healing, tumourigenesis, angiogenesis, apoptosis, inflammation, erythropoiesis, or hair loss.

39. A vector comprising a nucleic acid molecule as recited in any one of claims 36-38, for use in the diagnosis or therapy of a disease or abnormal physiological condition that is affected by hypoxia, such as cancer, ischaemic conditions, reperfusion injury, retinopathy, neonatal stress, preeclapmsia, atherosclerosis, inflammatory conditions, wound healing, tumourigenesis, angiogenesis, apoptosis, inflammation, erythropoiesis, or hair loss.

40. A ligand which binds specifically to, and which preferably inhibits the hypoxia-induced activity of, a polypeptide as recited in claim 35, for use in the diagnosis or therapy of tumourigenesis, angiogenesis, apoptosis, the biological response to hypoxia conditions, or a hypoxic-associated pathology.

41. A pharmaceutical composition suitable for modulating hypoxia and/or ischaemia, comprising a therapeutically-effective amount of a polypeptide as recited in any one of claims 13-21 or 35, a nucleic acid molecule according to any one of claims 22-24 or 36-38, a vector according to claim 25 or 39, or a ligand according to claim 30, 31 or 40, in conjunction with a pharmaceutically-acceptable carrier.

42. A pharmaceutical composition according to claim 41, wherein said pharmaceutically-acceptable carrier is a liposome.

43. A vaccine composition comprising a polypeptide as recited in any one of claims 13-21 or 35, a nucleic acid molecule as recited in any one of claims 22-24 or 36-38, or a vector according to claim 25 or 39.

44. A method of treating a disease in a patient in need of such treatment by administering to a patient a therapeutically effective amount of a polypeptide as recited in any one of claims 13-21 or 35, an antagonist of said polypeptide, or a nucleic acid molecule as recited in any one of claims 22-24 or 36-38.

45. A method of regulating tumourigenesis, angiogenesis, apoptosis, the biological response to hypoxia conditions, or a hypoxic-associated pathology in a patient in need of such treatment by administering to a patient a therapeutically effective amount of a polypeptide according to any one of claims 13-21 or 35, a nucleic acid molecule according to any one of claims 22-24 or 36-38, or a vector according to claim 25 or 39, or a ligand according to claim 30, 31 or 40 or a pharmaceutical composition according to claim 41 or 42.

46. A method according to claim 45, wherein, for diseases in which the expression of the natural gene or the activity of the polypeptide is lower in a diseased patient when compared to the level of expression or activity in a healthy patient, the polypeptide, nucleic acid molecule, ligand, compound or composition administered to the patient is an agonist.

47. A method according to claim 45, wherein, for diseases in which the expression of the natural gene or activity of the polypeptide is higher in a diseased patient when compared to the level of expression or activity in a healthy patient, the polypeptide, nucleic acid molecule, vector, ligand, compound or composition administered to the patient is an antagonist.

48. A polypeptide according to any one of claims 13-21 or 35, a nucleic acid molecule according to any one of claims 22-24 or 36-38, a vector according to claim 25 or 39, a ligand according to claim 30, 31 or 40 or a pharmaceutical composition according to claim 41 or 42, for use in the manufacture of a medicament for the treatment of a hypoxia-regulated condition.

49. A method of monitoring the therapeutic treatment of a disease or physiological condition in a patient, comprising monitoring over a period of time the level of expression or activity of polypeptide according to any one of claims 13-21 or 35, a nucleic acid molecule according to any one of claims 22-24 or 36-38, in tissue from said patient, wherein altering said level of expression or activity over the period of time towards a control level is indicative of regression of said disease.

50. A method of providing a hypoxia regulating gene, an apoptotic or an angiogenesis regulating gene by administering directly to a patient in need of such therapy an expressible vector comprising expression control sequences operably linked to one or more of the nucleic acid molecules recited in claims 22-24 or 36-38.

51. A method of diagnosing a hypoxia-regulated condition in a patient, comprising assessing the level of expression of a natural gene encoding a polypeptide according to any one of claims 13-21 or 35, or assessing the activity of such a polypeptide, in tissue from said patient and comparing said level of expression or activity to a control level, wherein a level that is different to said control level is indicative of the hypoxia-related condition.

52. A method according to claim 51 that is carried out *in vitro*.

53. A method according to claim 51 or claim 52, which comprises the steps of: (a) contacting a ligand according to claim 30, 31 or 40 with a biological sample under conditions suitable for the formation of a ligand-polypeptide complex; and (b) detecting said complex.

54. A method according to claim 51 or claim 52, comprising the steps of:

a) contacting a sample of tissue from the patient with a nucleic acid probe under stringent conditions that allow the formation of a hybrid complex between a nucleic acid molecule according to any one of claims 22-24 or 36-38 and the probe;

b) contacting a control sample with said probe under the same conditions used in step a); and

c) detecting the presence of hybrid complexes in said samples;

wherein detection of levels of the hybrid complex in the patient sample that differ from levels of the hybrid complex in the control sample is indicative of the hypoxia-related condition.

55. A method according to claim 51 or claim 52, comprising the steps of:

a) contacting a sample of nucleic acid from tissue of the patient with a nucleic acid primer under stringent conditions that allow the formation of a hybrid complex between a nucleic acid molecule according to any one of claims 22-24 or 36-38 and the primer;

b) contacting a control sample with said primer under the same conditions used in step a);

c) amplifying the sampled nucleic acid; and

d) detecting the level of amplified nucleic acid from both patient and control samples;

wherein detection of levels of the amplified nucleic acid in the patient sample that differ significantly from levels of the amplified nucleic acid in the control sample is indicative of the hypoxia-related condition.

56. A method according to claim 51 or claim 52, comprising the steps of:

a) obtaining a tissue sample from a patient being tested for the hypoxia-related condition;

b) isolating a nucleic acid molecule according to any one of claims 22-24 or 36-38 from said tissue sample; and

c) diagnosing the patient for disease by detecting the presence of a mutation which is associated with the hypoxia-related condition in the nucleic acid molecule as an indication of the hypoxia-related condition.

57. The method of claim 56, further comprising amplifying the nucleic acid molecule to form an amplified product and detecting the presence or absence of a mutation in the amplified product.

58. A method according to any one of claims 49-57, wherein said disease is cancer, ischaemic conditions, reperfusion injury, retinopathy, neonatal stress, preeclapmsia, atherosclerosis, inflammatory

conditions, wound healing, tumourigenesis, angiogenesis, apoptosis, inflammation, erythropoiesis, or hair loss.

59. A method according to claim 58, wherein said hypoxia or ischaemia-related tissue damage is due to a disorder of the cerebral, coronary or peripheral circulation.

60. A method according to any one of claims 49, and 54-59, wherein the tissue is a cancer tissue.

61. A method for the identification of a compound that is effective in the treatment and/or diagnosis of disease, comprising contacting a polypeptide according to any one of claims 13-21 or 35, a nucleic acid molecule according to any one of claims 22-24 or 36-38 with one or more compounds suspected of possessing binding affinity for said polypeptide or nucleic acid molecule, and selecting a compound that binds specifically to said nucleic acid molecule or polypeptide.

62. A method for the identification of a compound that is effective in the treatment and/or diagnosis of disease, comprising contacting a cell or cell membrane preparation comprising a polypeptide according to any one of claims 13-21 or 35 or a nucleic acid molecule according to any one of claims 22-24 or 36-38 with one or more candidate compounds and detecting the degree of compound binding, or the stimulation or inhibition of a functional response in said cell or cell membrane.

63. A compound identified or identifiable by a method according to claim 61 or claim 62.

64. A compound according to claim 63, which is a natural or modified substrate, an enzyme, a receptor, a small organic molecule, such as a small natural or synthetic organic molecule of up to 2000Da, preferably 800Da or less, a peptidomimetic, an inorganic molecule, a peptide, a polypeptide, an antibody, or a structural or functional mimetics of any of these compounds.

65. A kit useful for diagnosing disease comprising a first container containing a nucleic acid probe that hybridises under stringent conditions with a nucleic acid molecule according to any one of claims 22-24 or 36-38; a second container containing primers useful for amplifying said nucleic acid molecule; and instructions for using the probe and primers for facilitating the diagnosis of disease.

66. The kit of claim 65, further comprising a third container holding an agent for digesting unhybridised RNA.

67. An array of at least two nucleic acid molecules, wherein each of said nucleic acid molecules either corresponds to the sequence of, is complementary to the sequence of, or hybridises specifically to a nucleic acid molecule according to any one of claims 22-24 or 36-38.

68. An array according to claim 67, which contains nucleic acid molecules that either correspond to the sequence of, are complementary to the sequence of, or hybridise specifically to at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 92a, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294 or 295 of the nucleic acid molecules implicated in a hypoxia-regulated condition as recited in claims 22-24 or 36-38.

69. An array according to any claim 67 or claim 68, wherein said nucleic acid molecules consist of between twelve and two thousand nucleotides.

70. An array of antibodies, comprising at least two different antibody species, wherein each antibody species is immunospecific with a polypeptide implicated in a hypoxia-regulated condition as recited in any one of claims 13-21 or 35.

71. An array of polypeptides, comprising at least two polypeptide species as recited in any one of claims 13-21 or 35, wherein each polypeptide species is implicated in a hypoxia-regulated condition, or is a functional equivalent variant or fragment thereof.

72. A kit comprising an array of nucleic acid molecules according to any one of claims 67-69.

73. A kit comprising one or more antibodies that bind to a polypeptide as recited in any one of claims 13-21 or 35; and a reagent useful for the detection of a binding reaction between said antibody and said polypeptide.

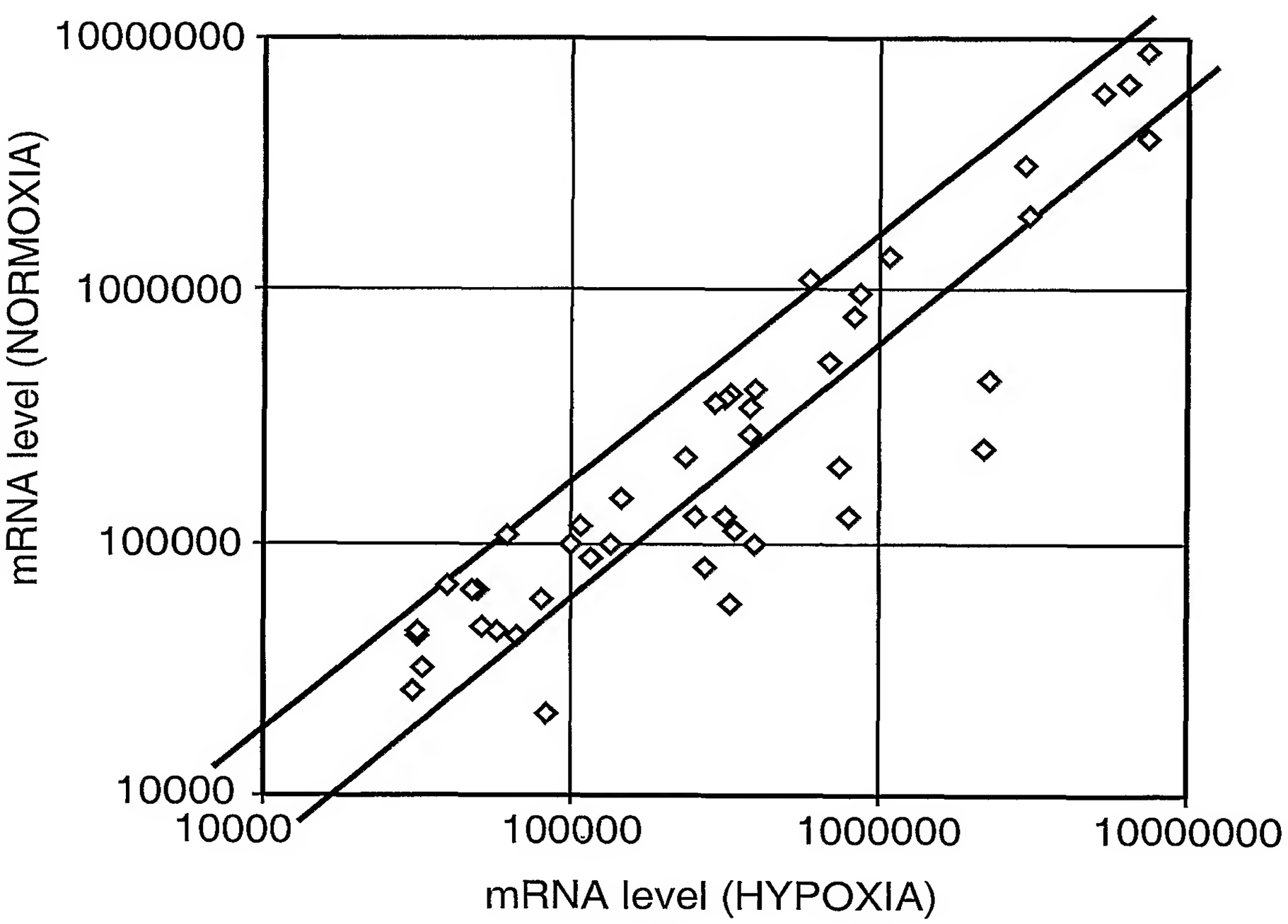
74. A transgenic or knockout non-human animal that has been transformed to express higher, lower or absent levels of a polypeptide according to any one of claims 13-21 or 35.

75. A method for screening for a compound effective to treat disease, by contacting a non-human transgenic animal according to claim 74 with a candidate compound and determining the effect of the compound on the disease or physiological condition of the animal.

76. A substantially purified polypeptide comprising the consensus sequence: KAMVACYPGNGTGYVRHVDNPNGDGRCITCIYYLNKNWDAKLHGGILRIFPEGKSFIADVEPI FDRLLFFWSDRRNPHEVQPSYATRYAMTVWYFDAEERAEAKKK, or a variant thereof.

77. A substantially purified polypeptide according to claim 76, for use in the diagnosis or treatment of a hypoxia-related disease or condition.

FIG. 1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100000
1000000
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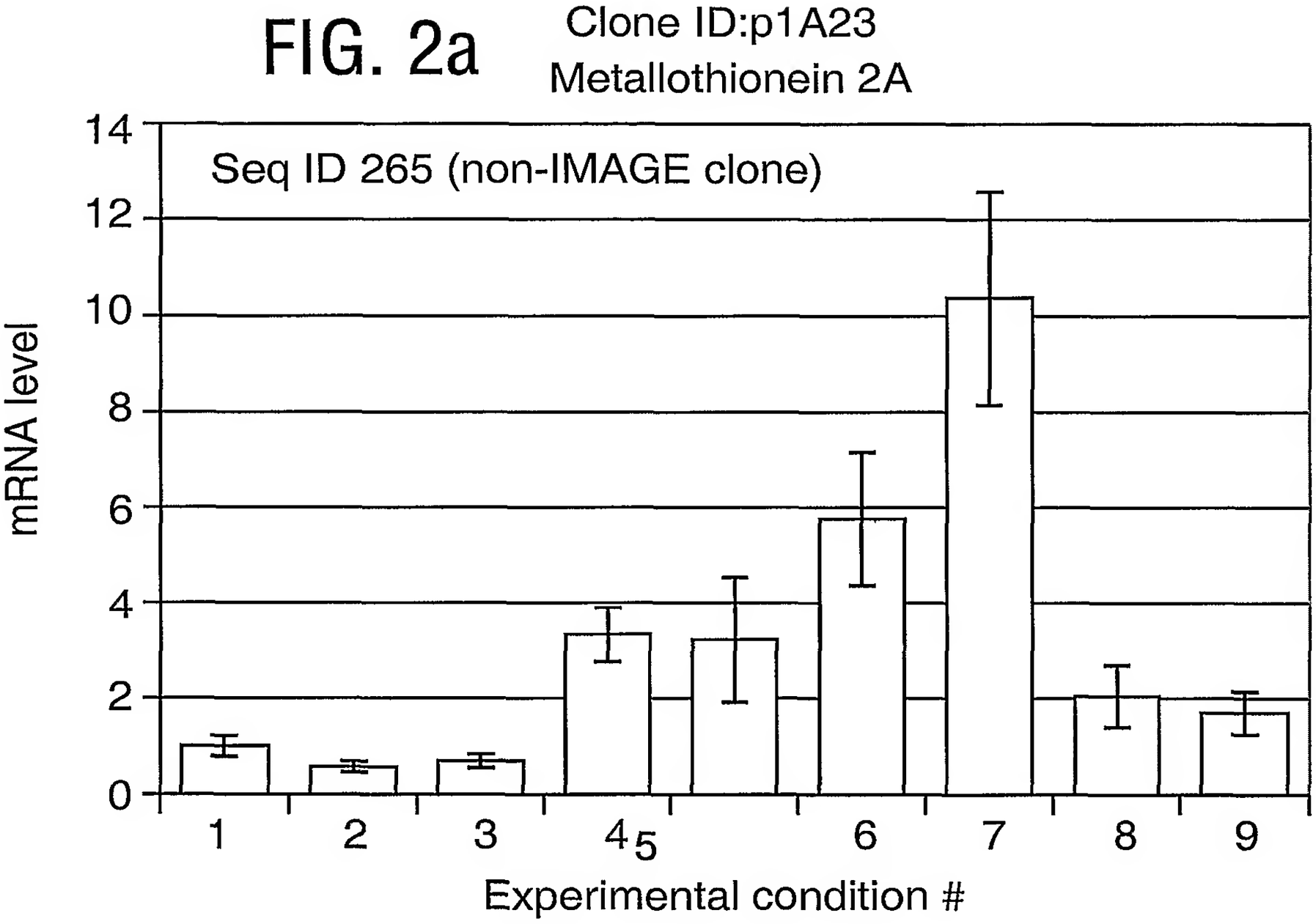
FIG. 2a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10
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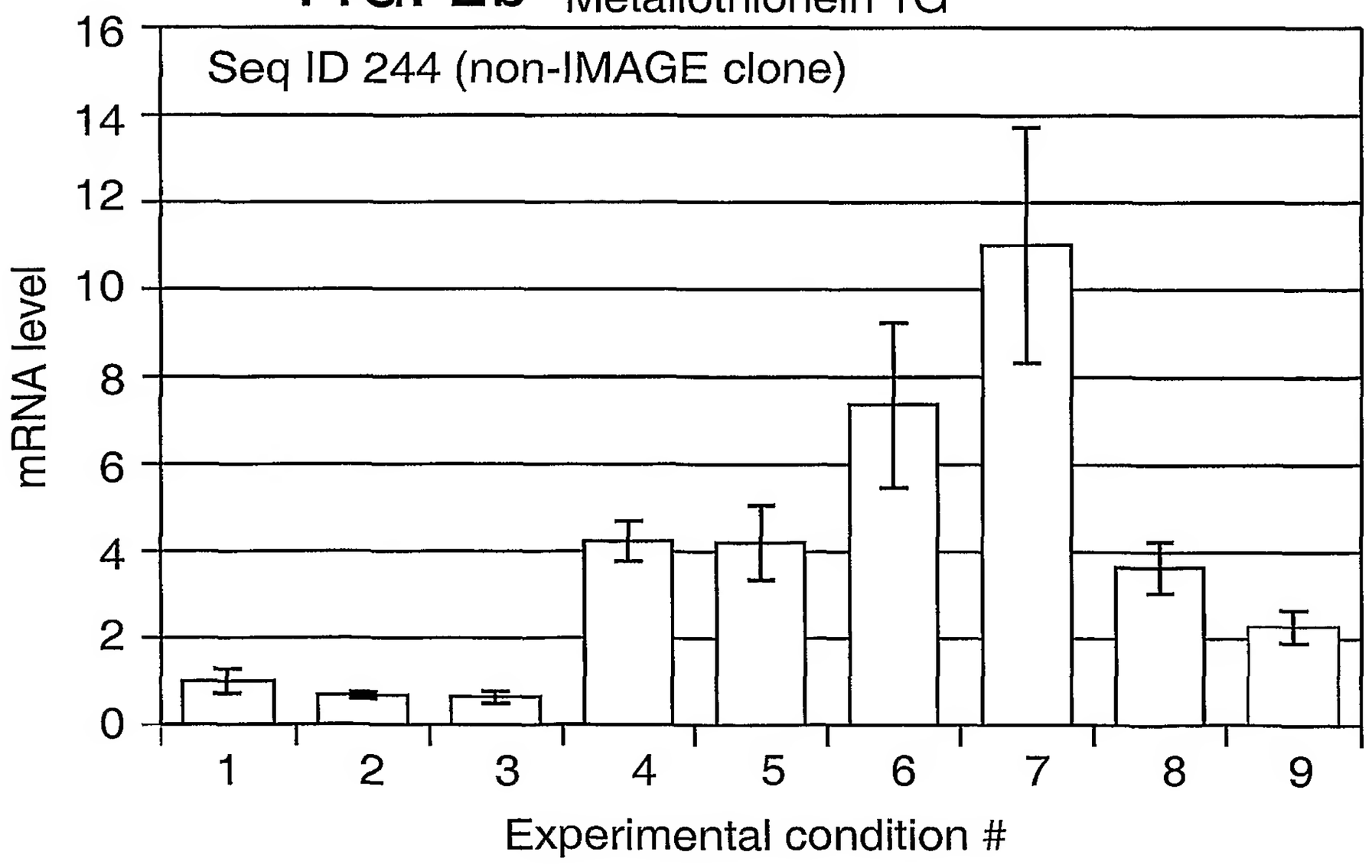
3
4
5
6
7
8
9
Experimental condition #

FIG. 2b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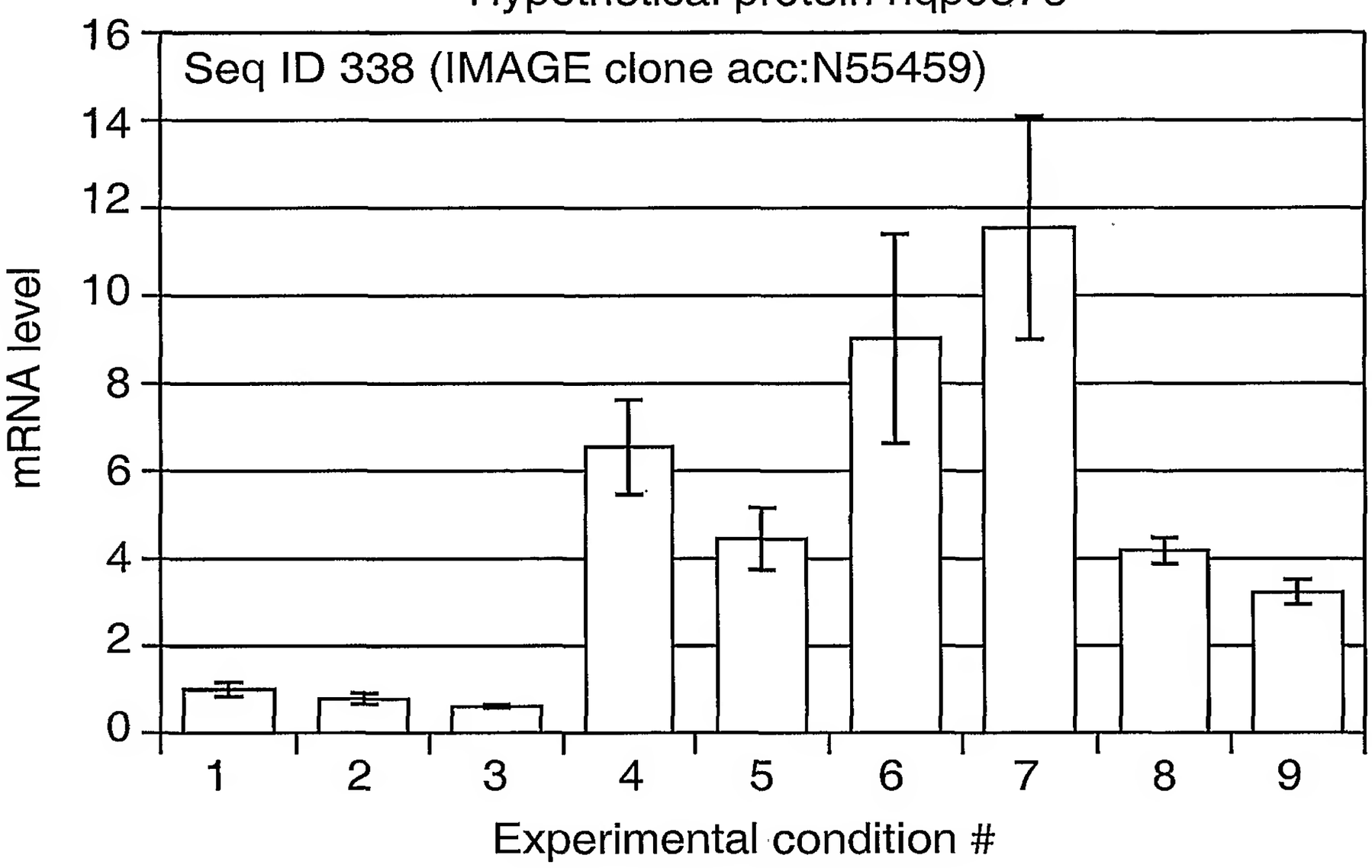
4
5
6
7
8
9
Experimental condition #

FIG. 2c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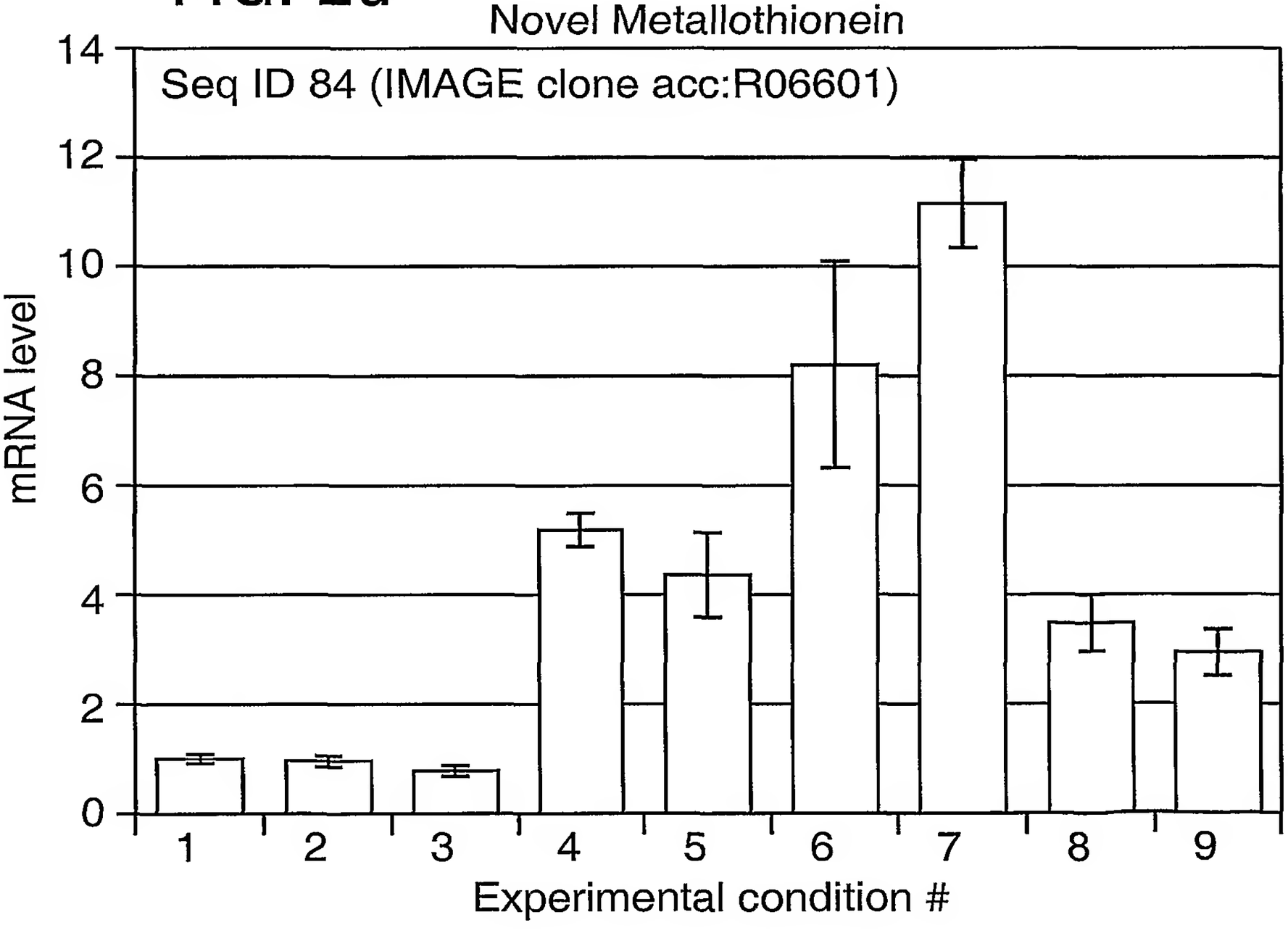
3
4
5
6
7
8
9
Experimental condition #

FIG. 2d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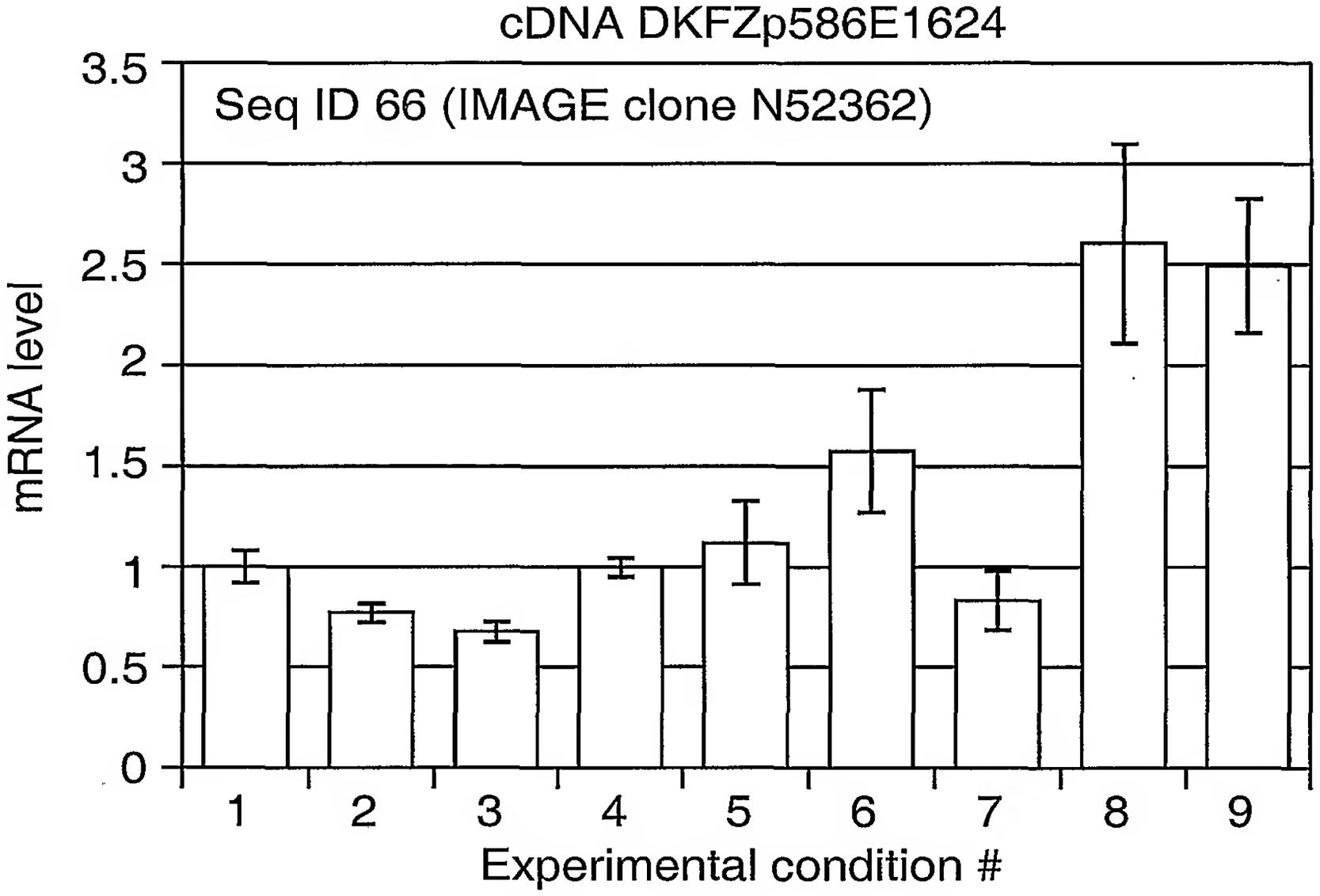
5
6
7
8
9
Experimental condition #

FIG.3a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2.5
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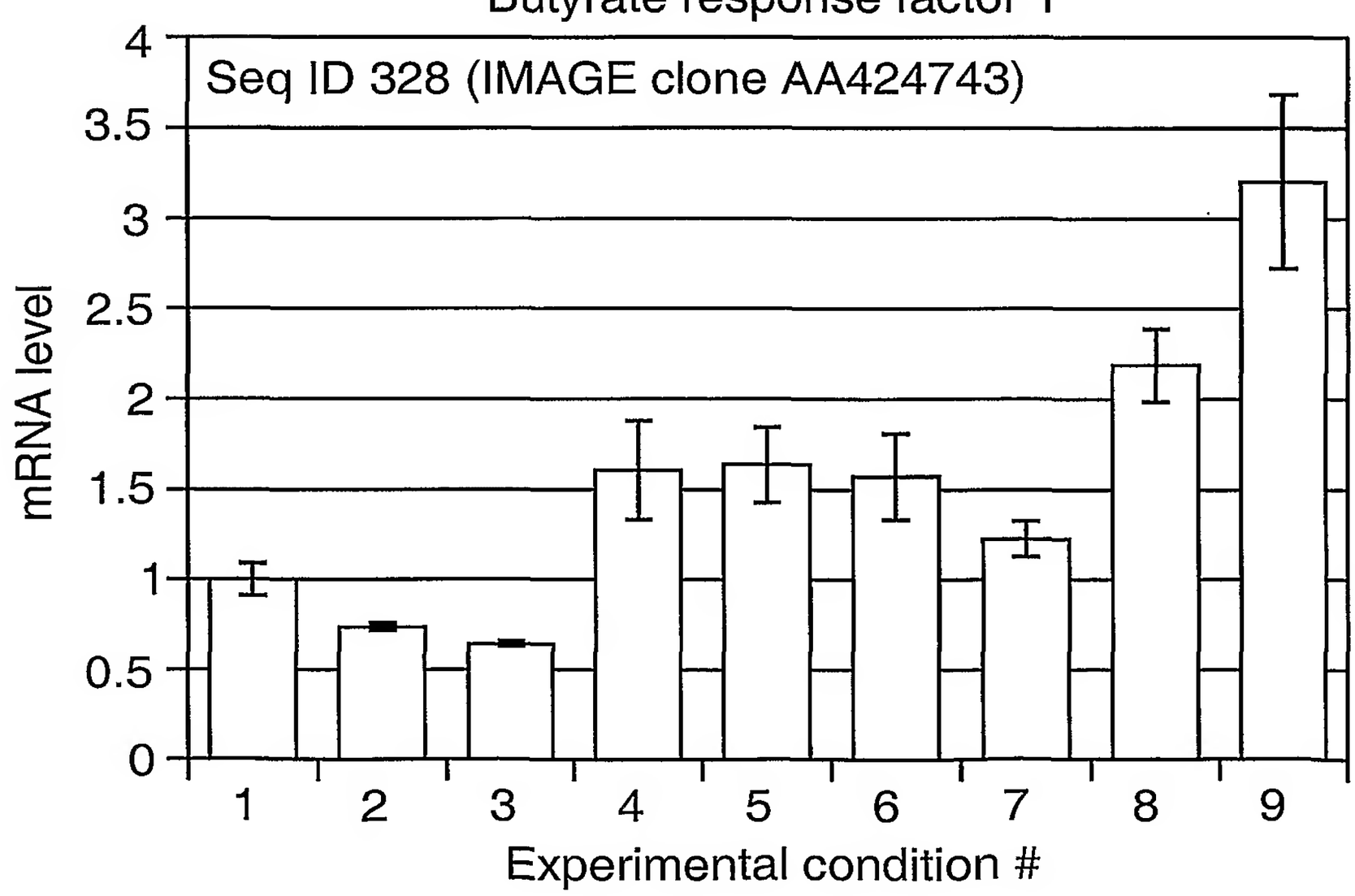
1.5
1
0.5
0
1
2
3
4
5
6
7
8
9
Experimental condition #

FIG. 3b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3.5
3
2.5
2
1.5
1
0.5
0
1
2
3
4
5
6
7
8
9
Experimental condition #

FIG .3c

Clone p1D1

Hypothetical protein FLJ10134

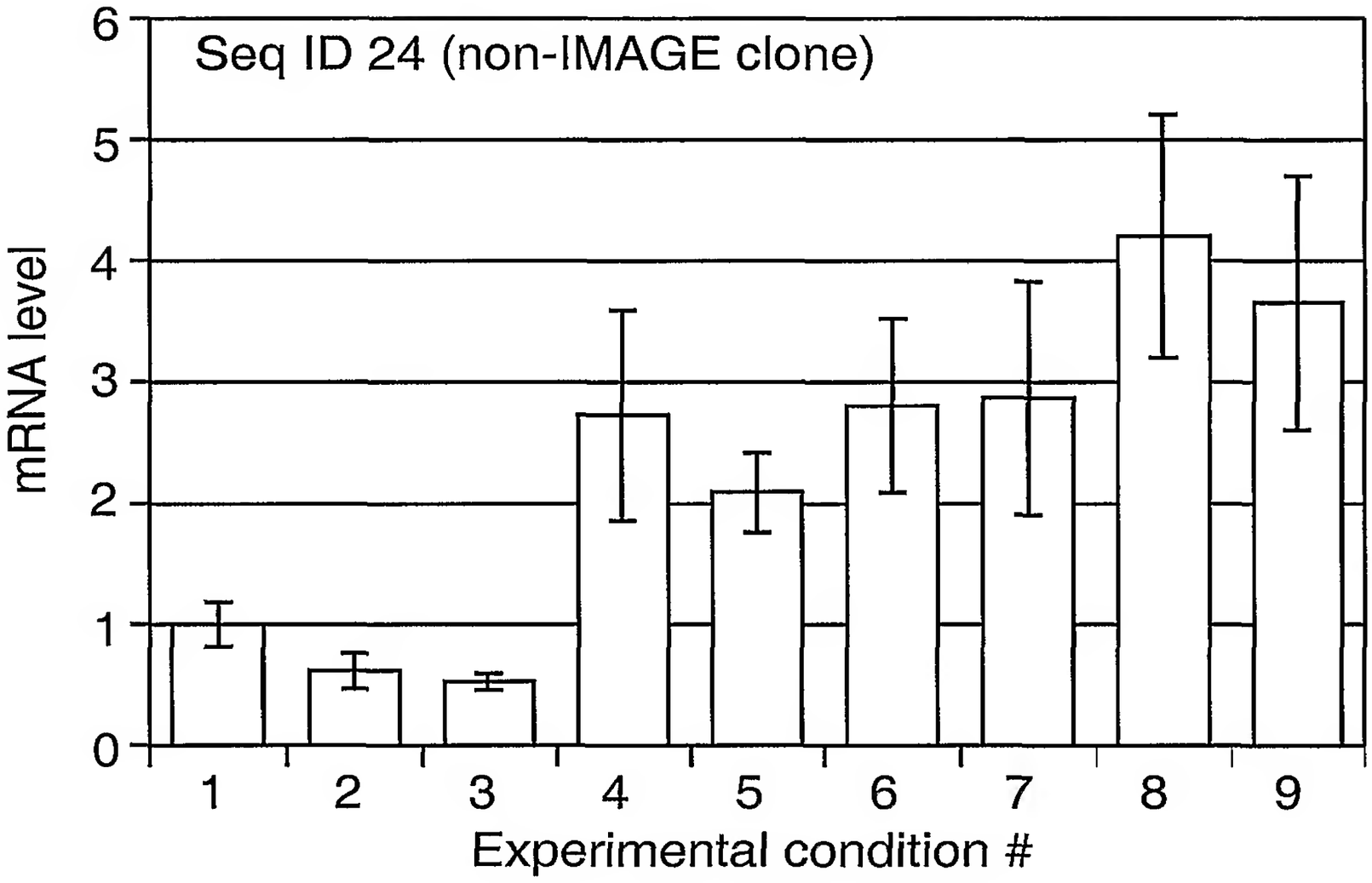


FIG .3d

Clone p1D2

Hypothetical protein FLJ10134

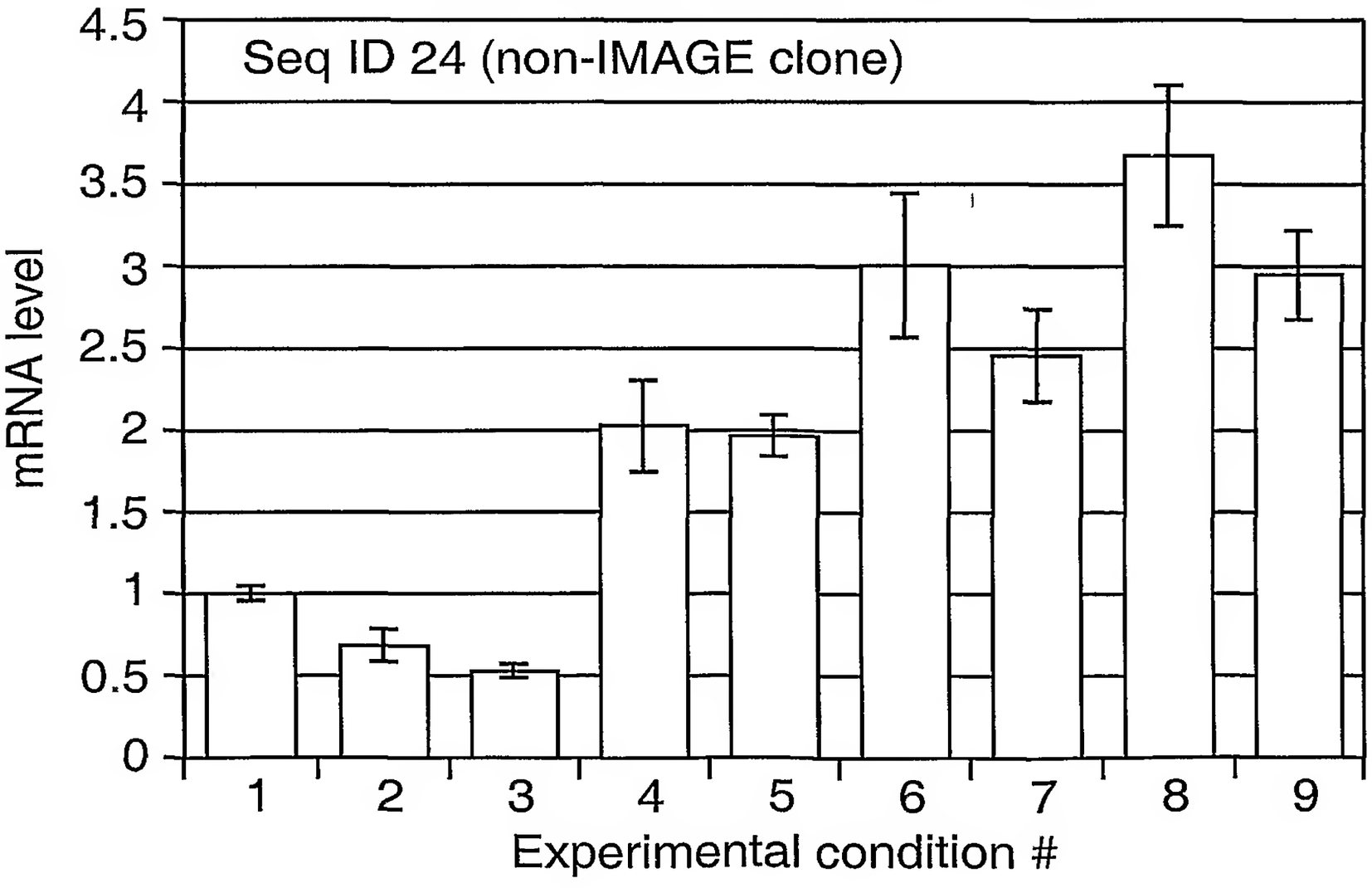


FIG .3e

Clone p1D6
ERO1 (S. cerevisiae)-like

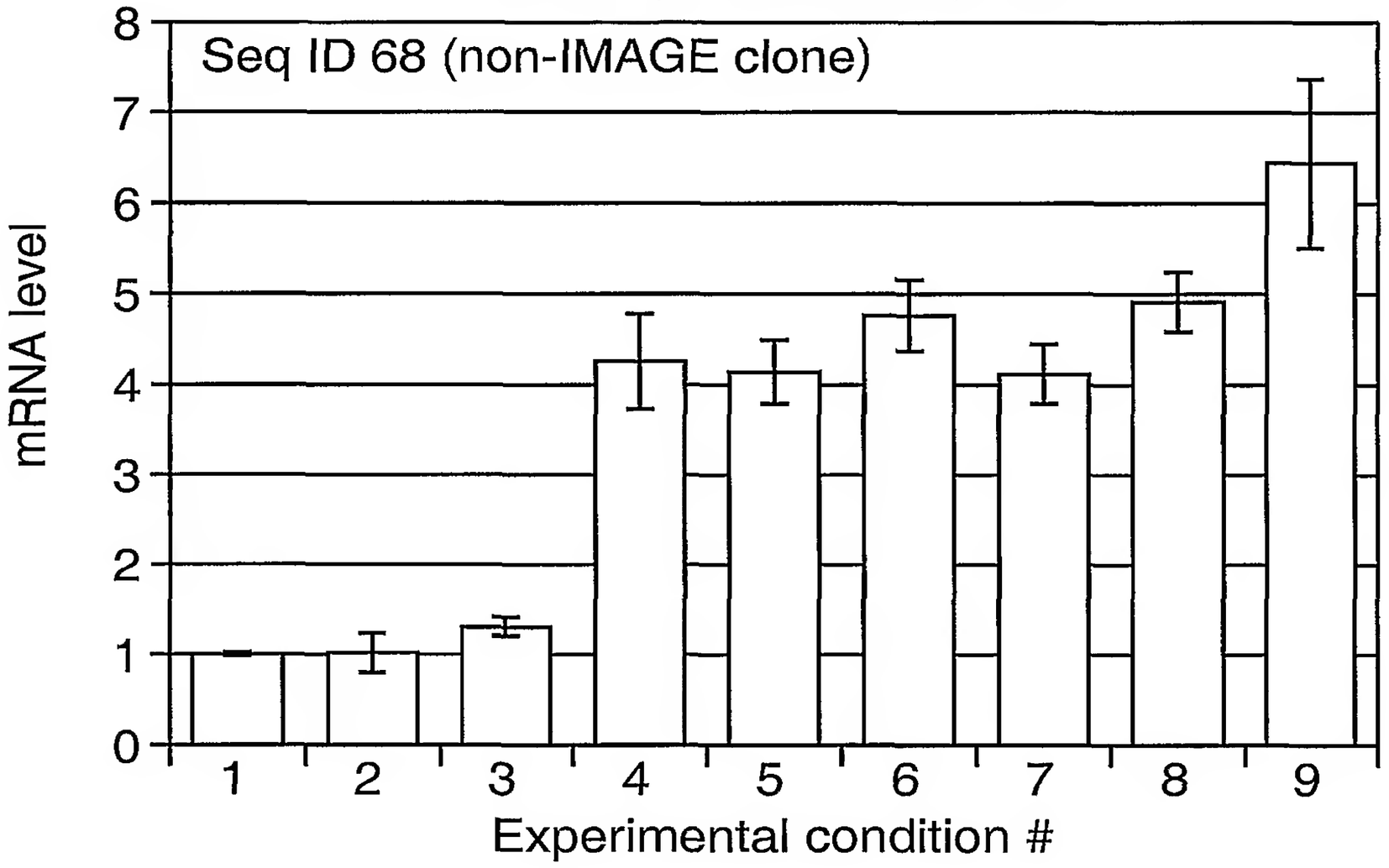


FIG .3f

Clone p1E6
EGL nine (C.elegans) homolog

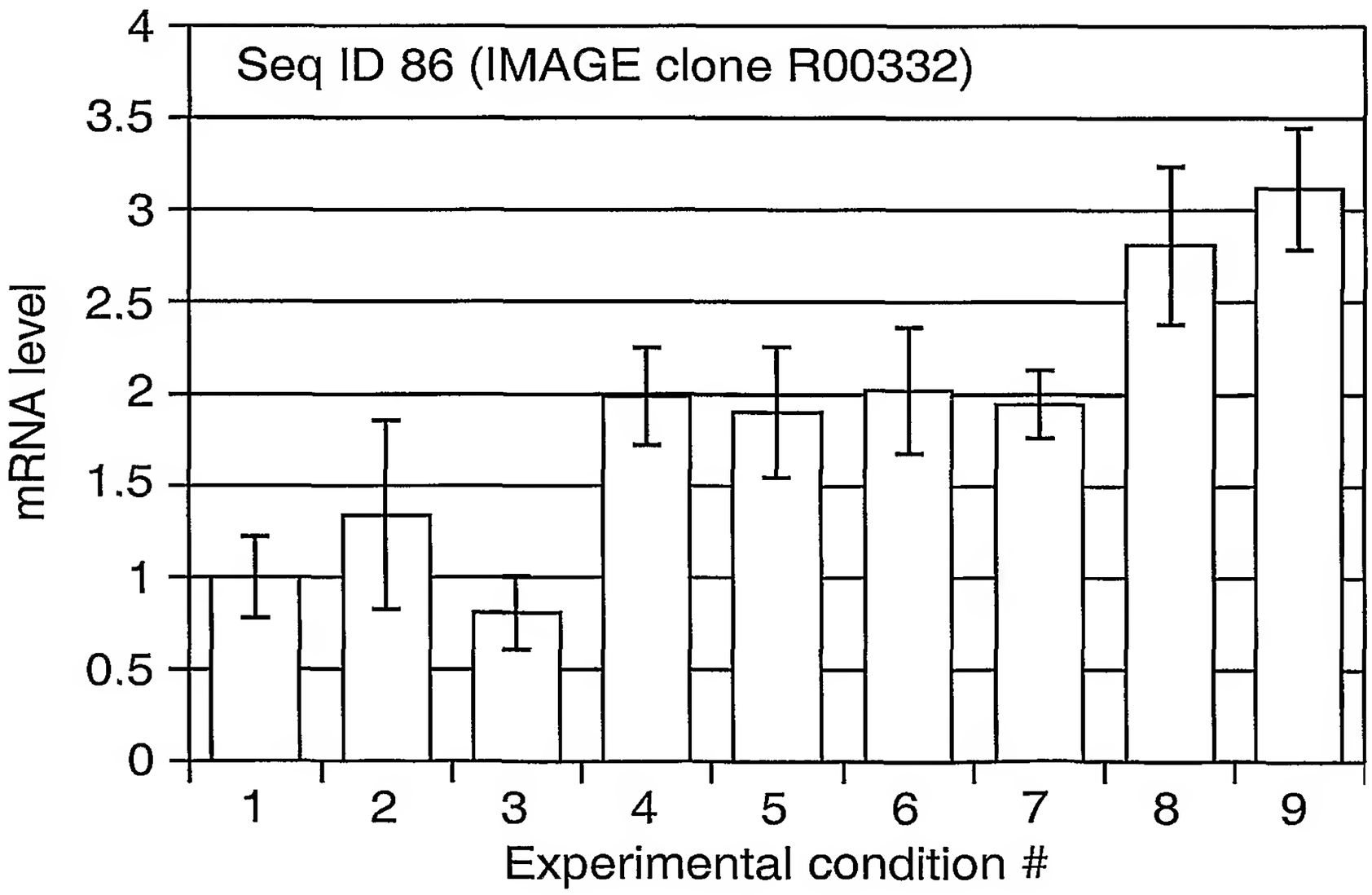


FIG .4

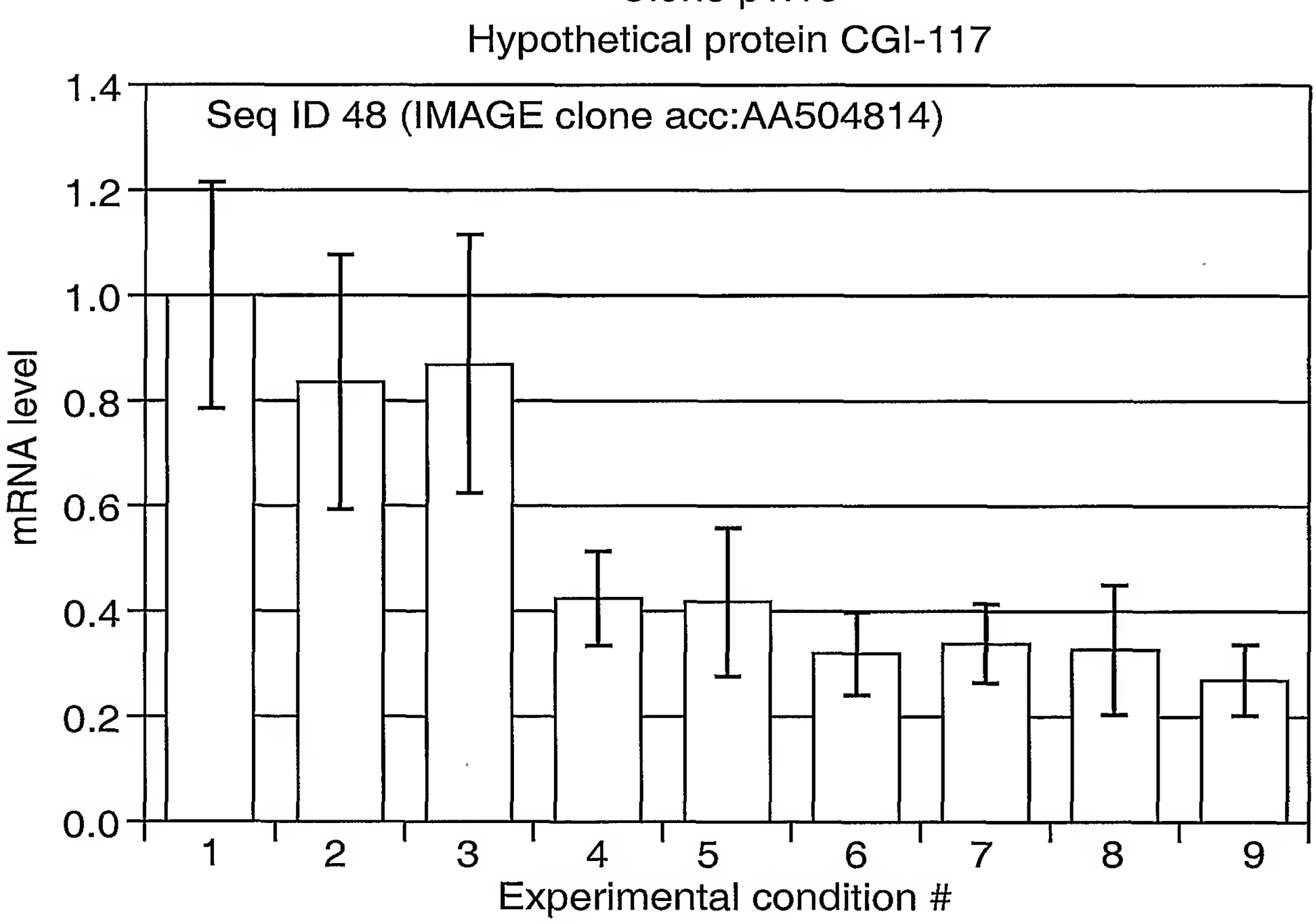

Clone p1I15
Hypothetical protein CGI-117
Seq ID 48 (IMAGE clone acc:AA504814)
mRNA level
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
1
2
3
4
5
6
7
8
9
Experimental condition #

FIG. 5

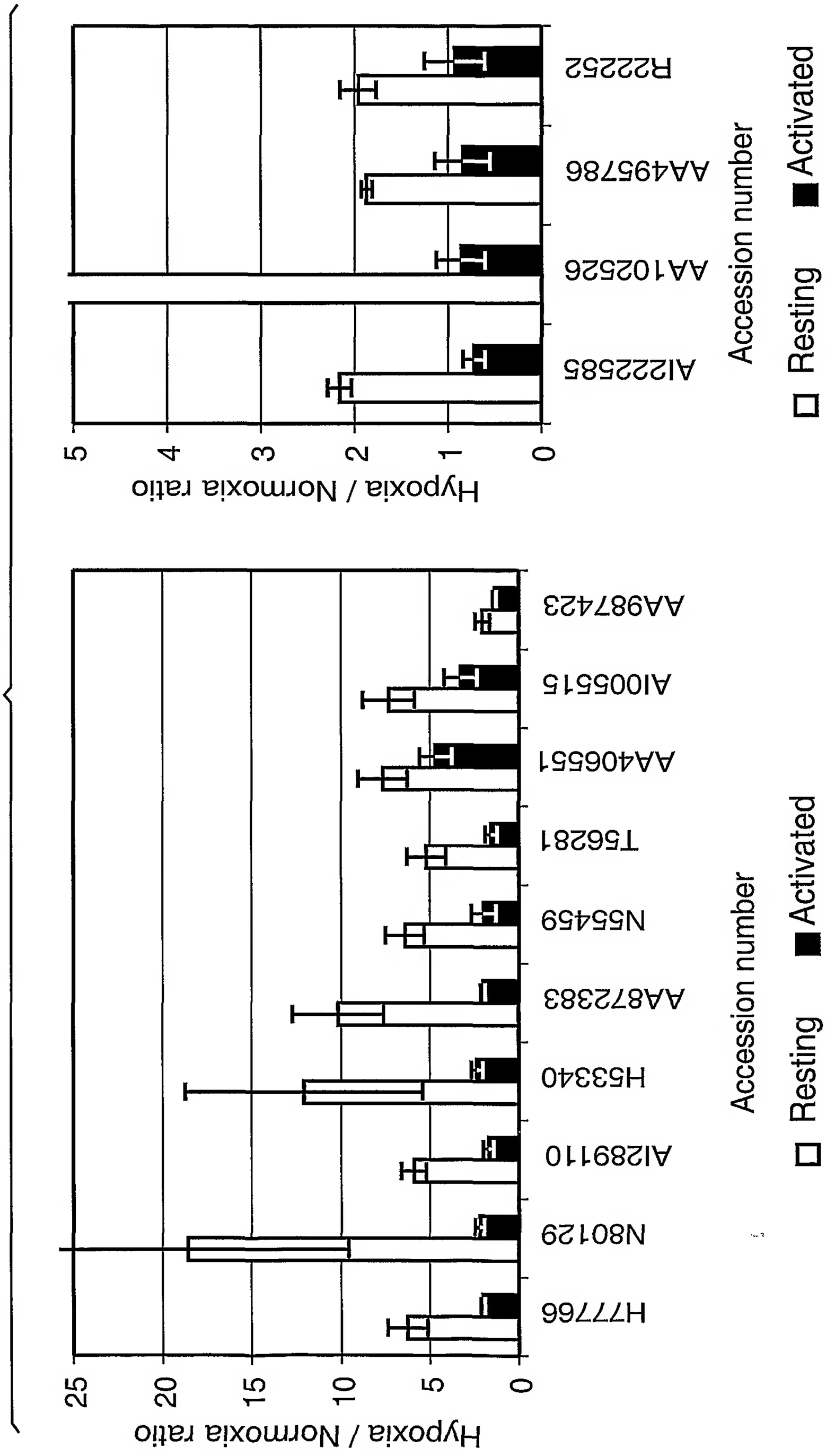

Hypoxia / Normoxia ratio
0
1
2
3
4
5
R22252
AA495786
AA102526
AI222585
Accession number
Resting
Activated
Hypoxia / Normoxia ratio
0
5
10
15
20
25
AA987423
AI005515
AA406551
T56281
N55459
AA872383
H53340
AI289110
N80129
H77766
Accession number
Activated
Resting

FIG. 6

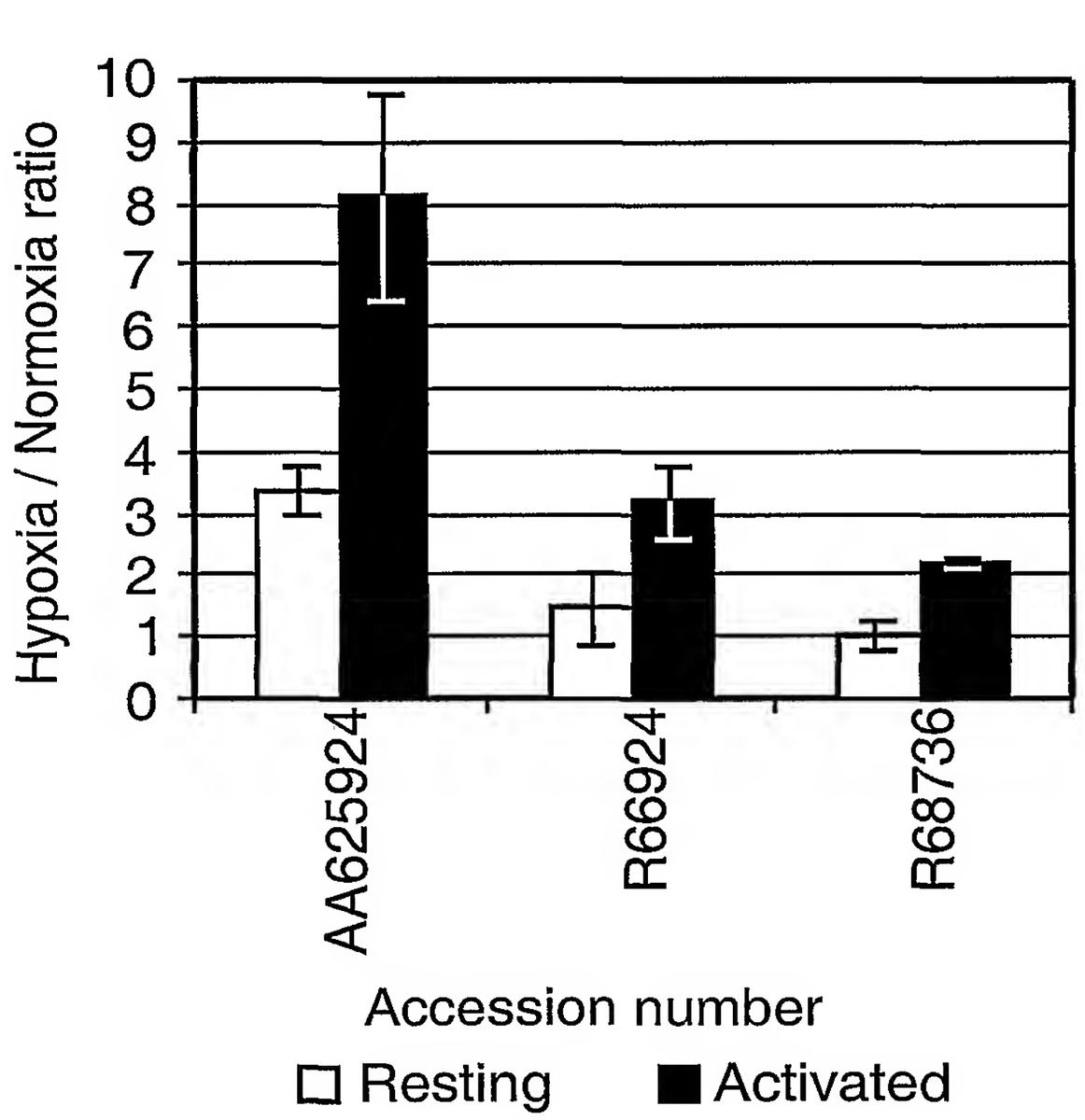

Hypoxia / Normoxia ratio
0
1
2
3
4
5
6
7
8
9
10
AA625924
R66924
R68736
Accession number
Resting
Activated

FIG. 7

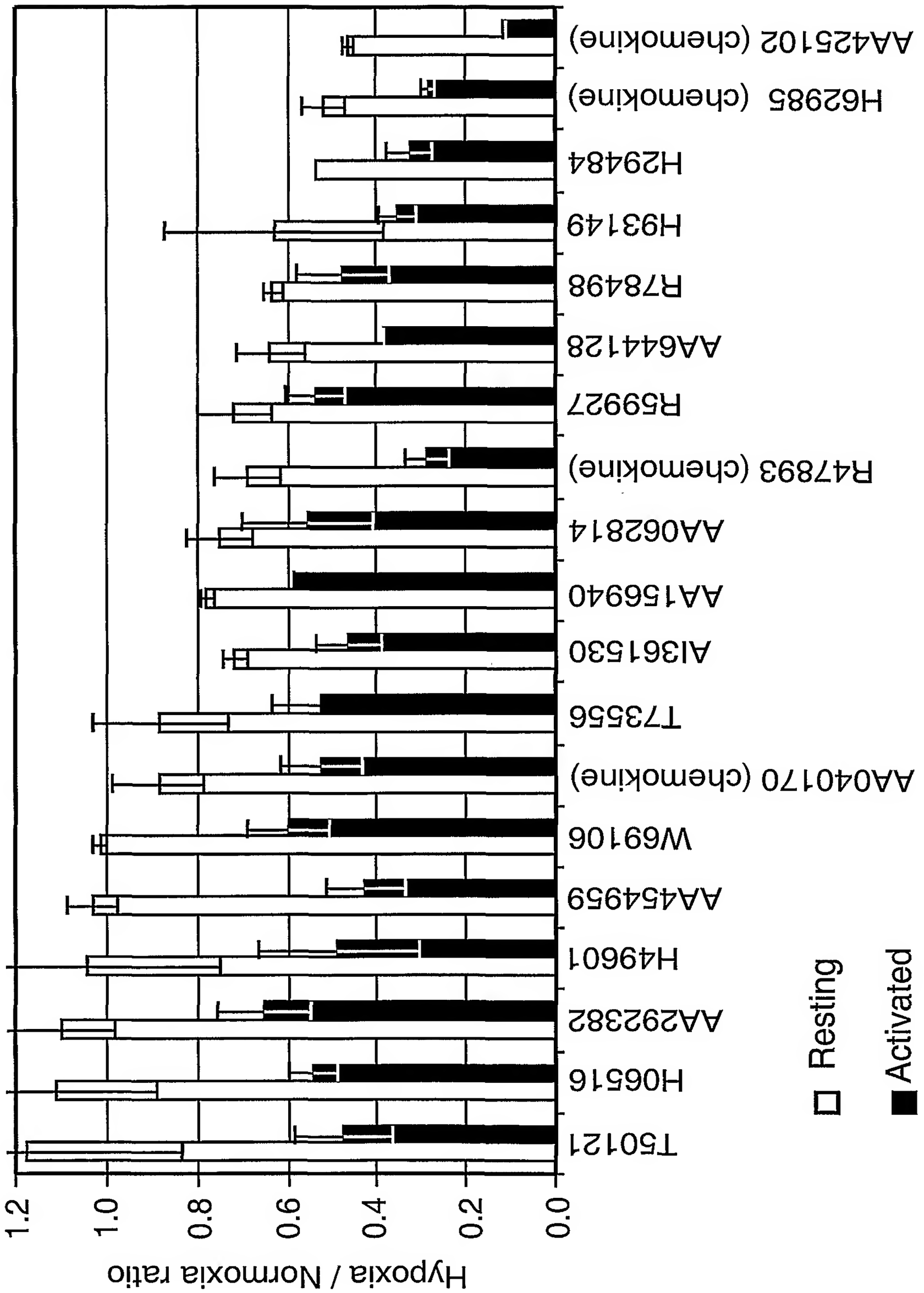
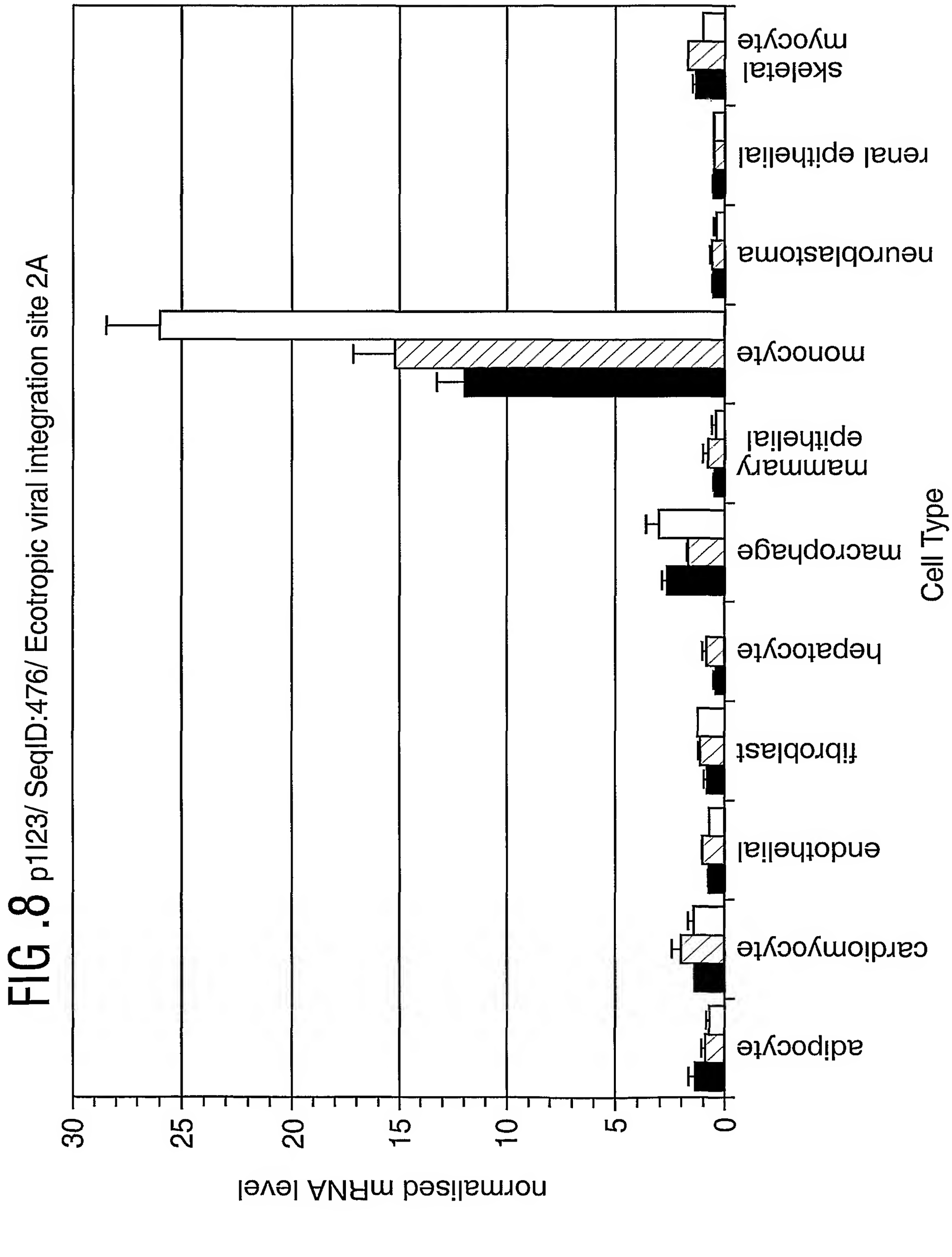

Hypoxia / Normoxia ratio
1.2
1.0
0.8
0.6
0.4
0.2
0.0
Accession number
T50121
H06516
AA292382
H49601
AA549459
W69106
AA401170 (chemokine)
T73556
AI361530
AA156940
AA062814
R47893 (chemokine)
R59927
AA644128
R78498
H93149
H29484
H62985 (chemokine)
AA425102 (chemokine)
Resting
Activated

FIG .8 p1I23/ SeqID:476/ Ecotropic viral integration site 2A



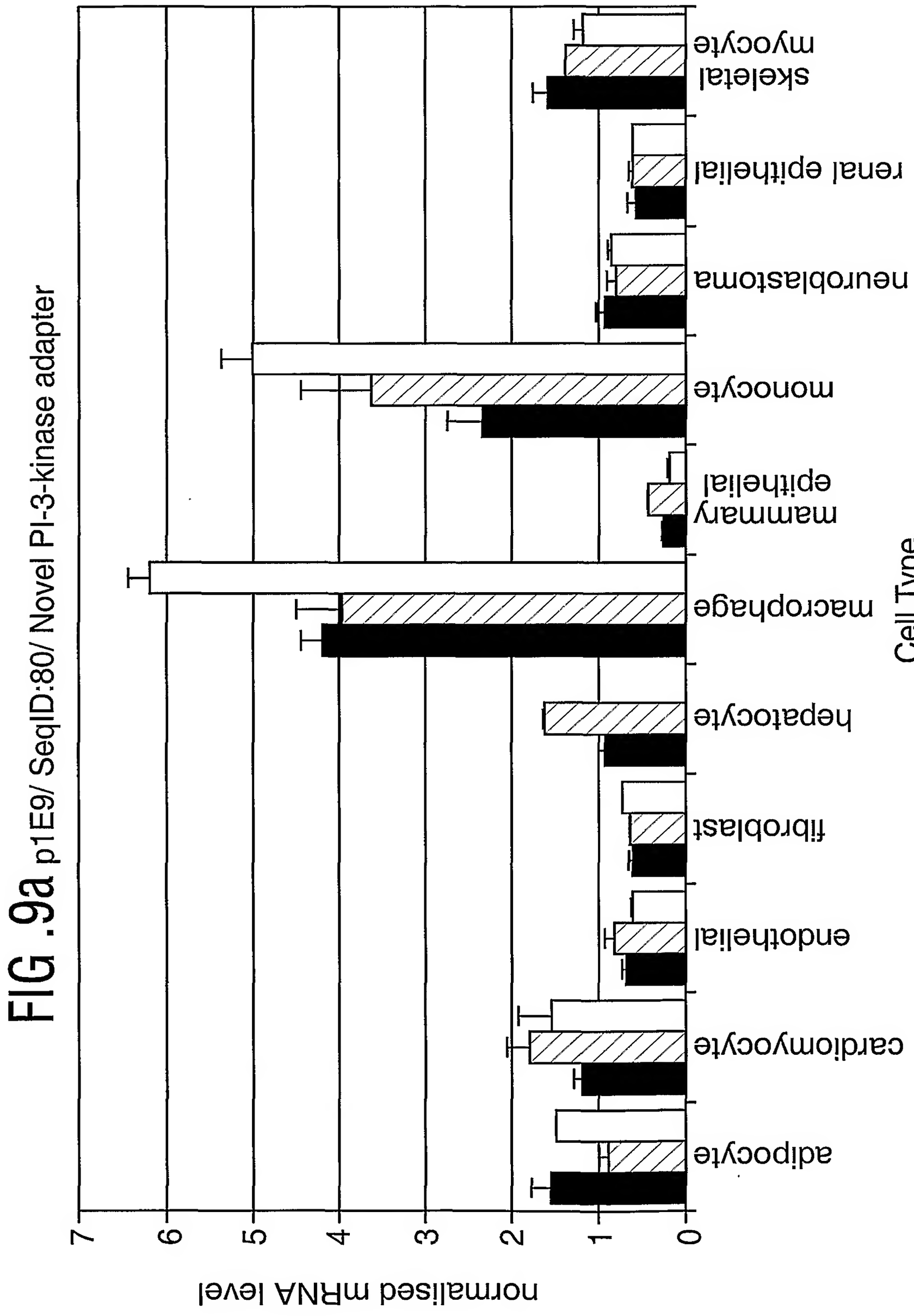


FIG .9a p1E9/ SeqID:80/ Novel PI-3-kinase adapter
normalised mRNA level
0
1
2
3
4
5
6
7
Cell Type
adipocyte
cardiomyocyte
endothelial
fibroblast
hepatocyte
macrophage
mammary epithelial
monocyte
neuroblastoma
renal epithelial
skeletal myocyte
normoxia
6hr hypoxia
18hr hypoxia

FIG. 9b p1E9/ SeqID:80/ Novel PI-3-kinase adapter

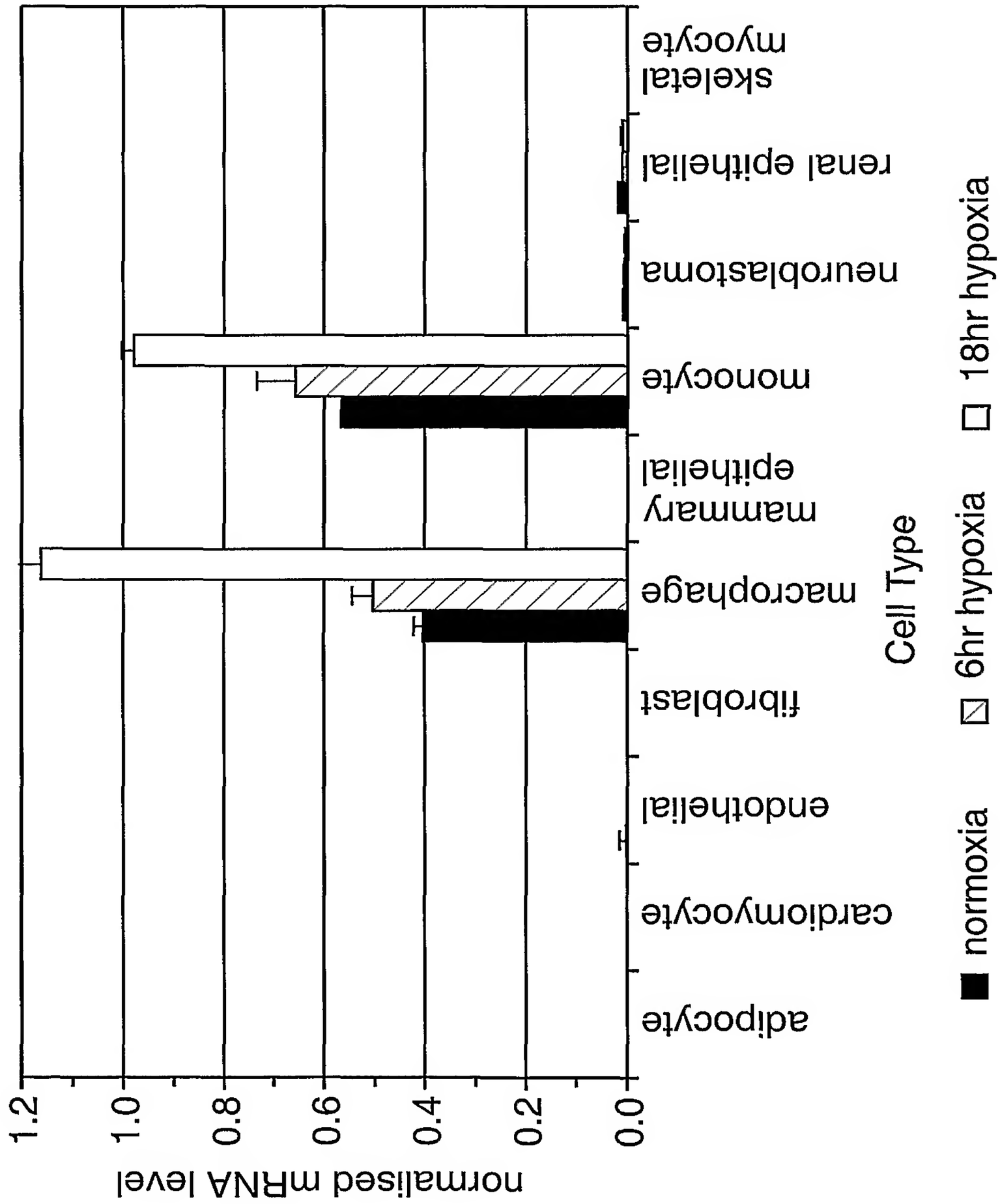


FIG. 9C p1N15/ IMAGE clone acc: R59598/ Syk

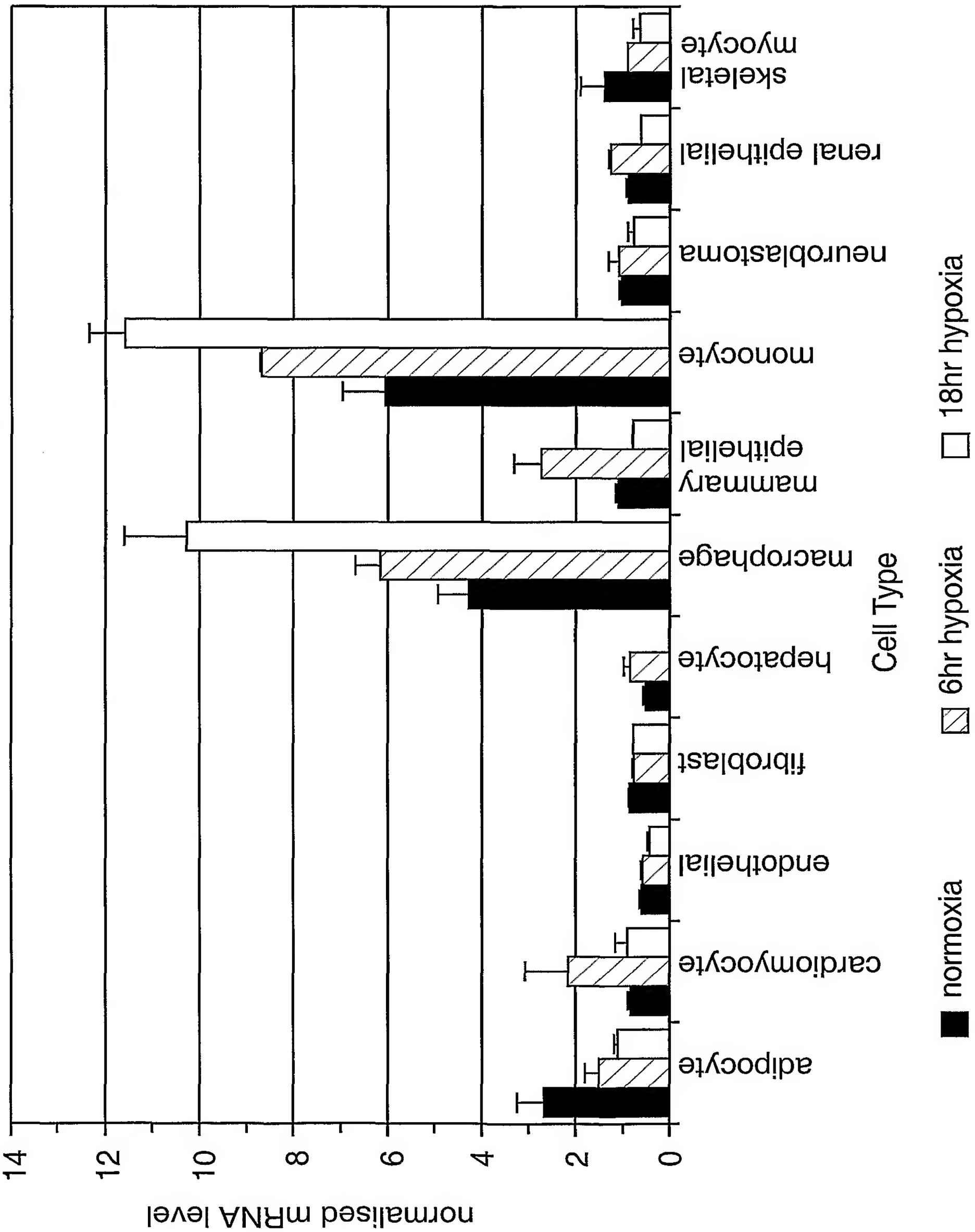


FIG .10 p1C10/ SeqID:376/ Regulator of G-protein signalling 1

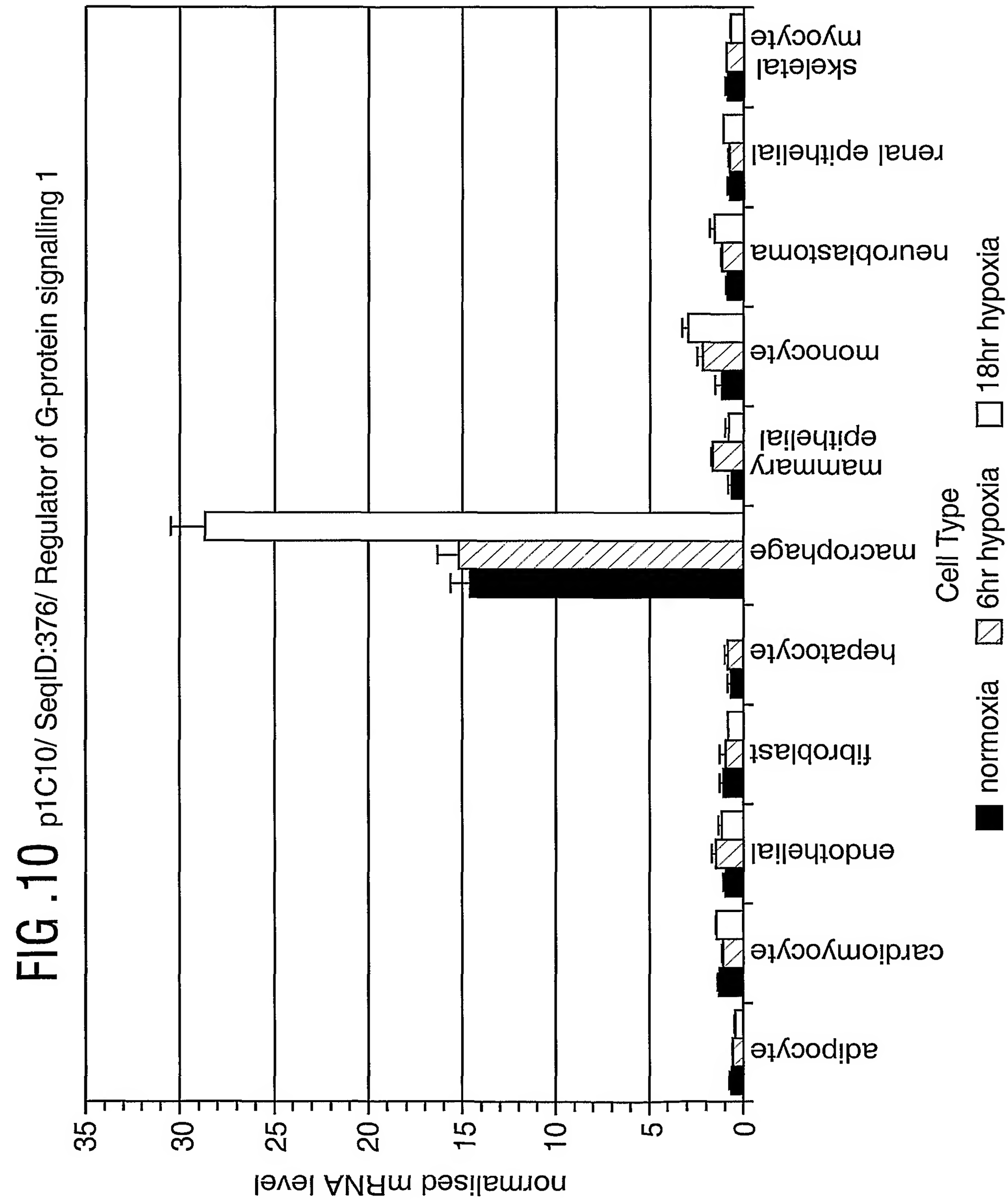


FIG 11 p1C19/ SeqID:390/ GM2 ganglioside activator protein

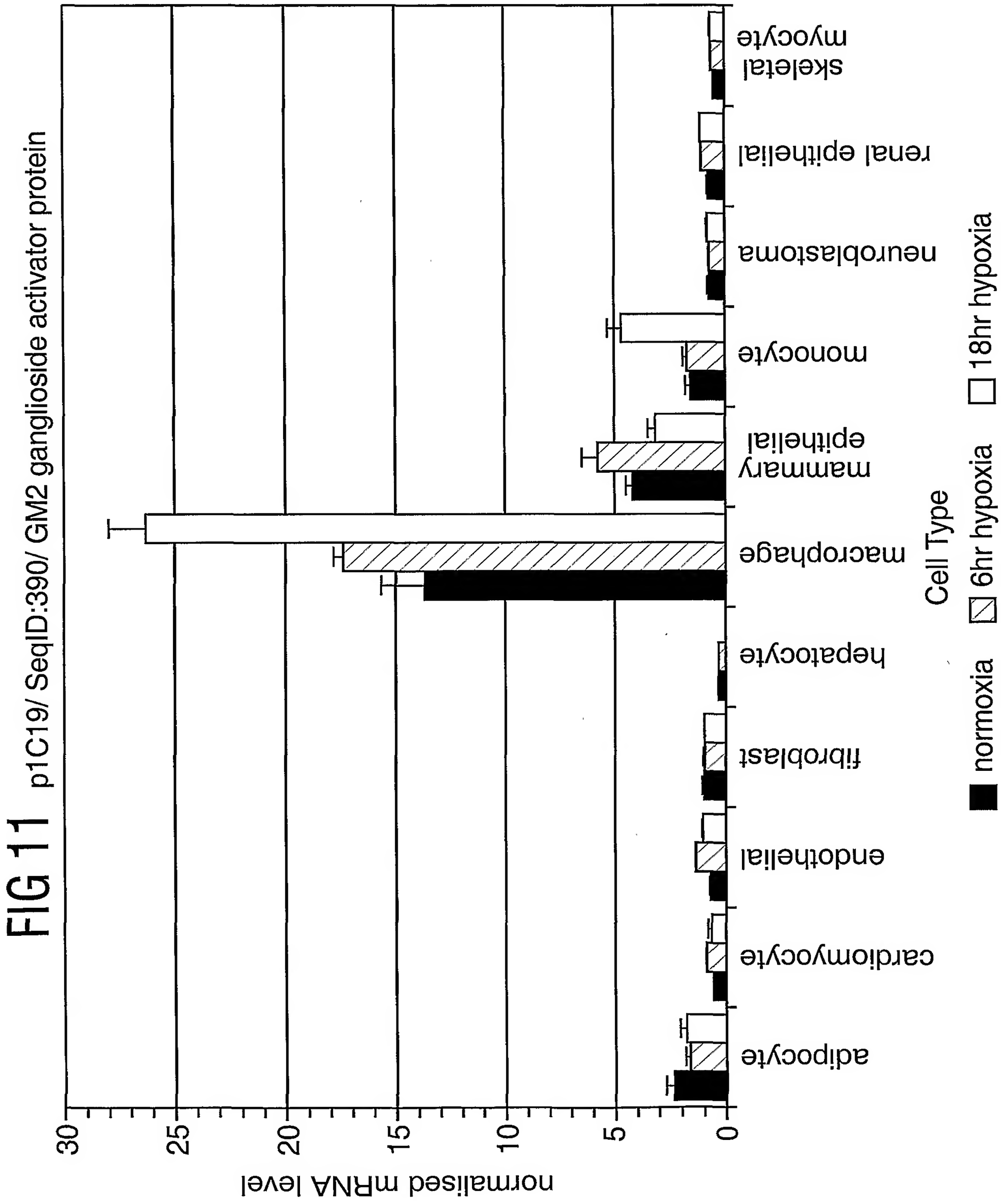


FIG .12 p1E13/ SeqID:22/ Hypothetical protein PRO0823

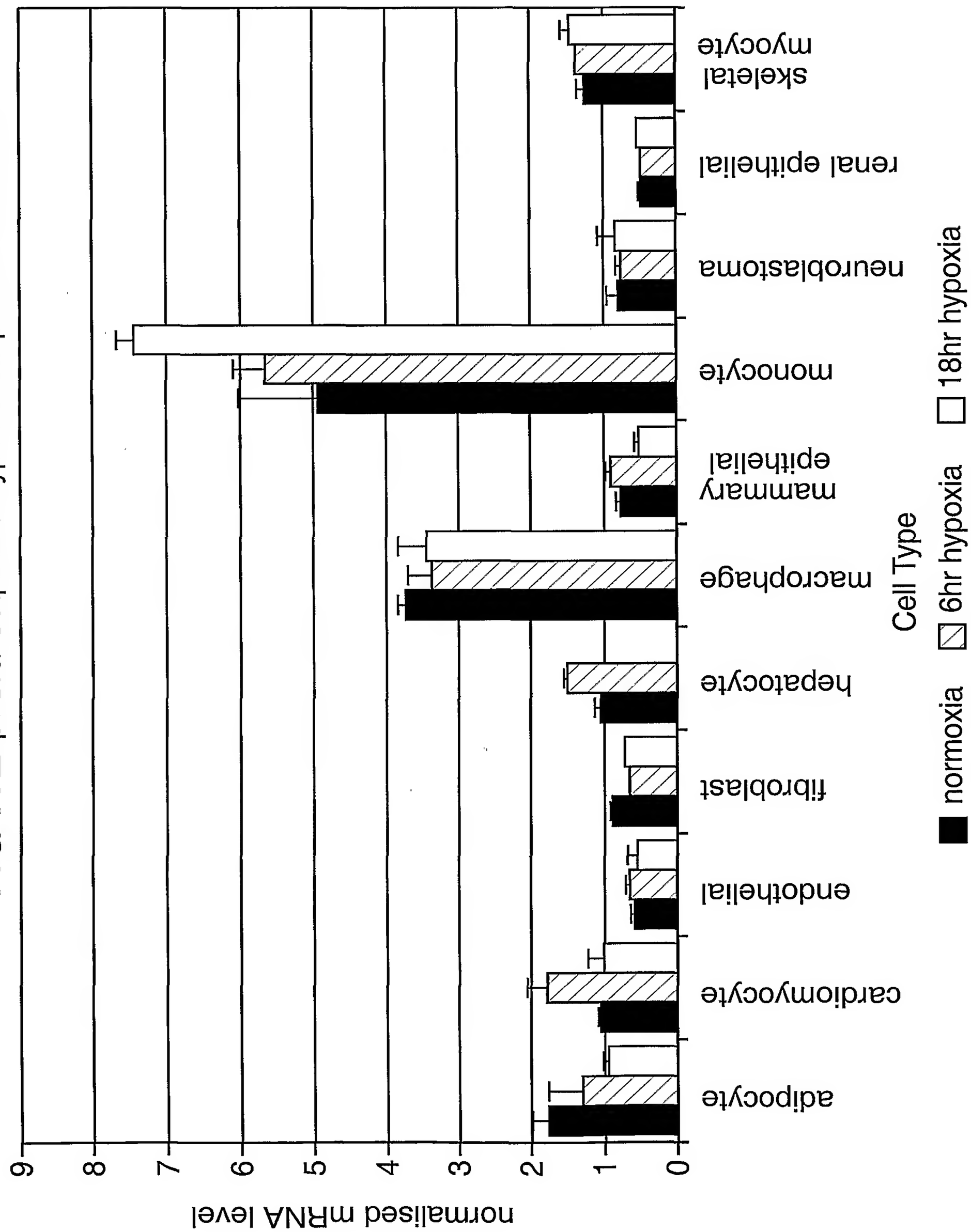
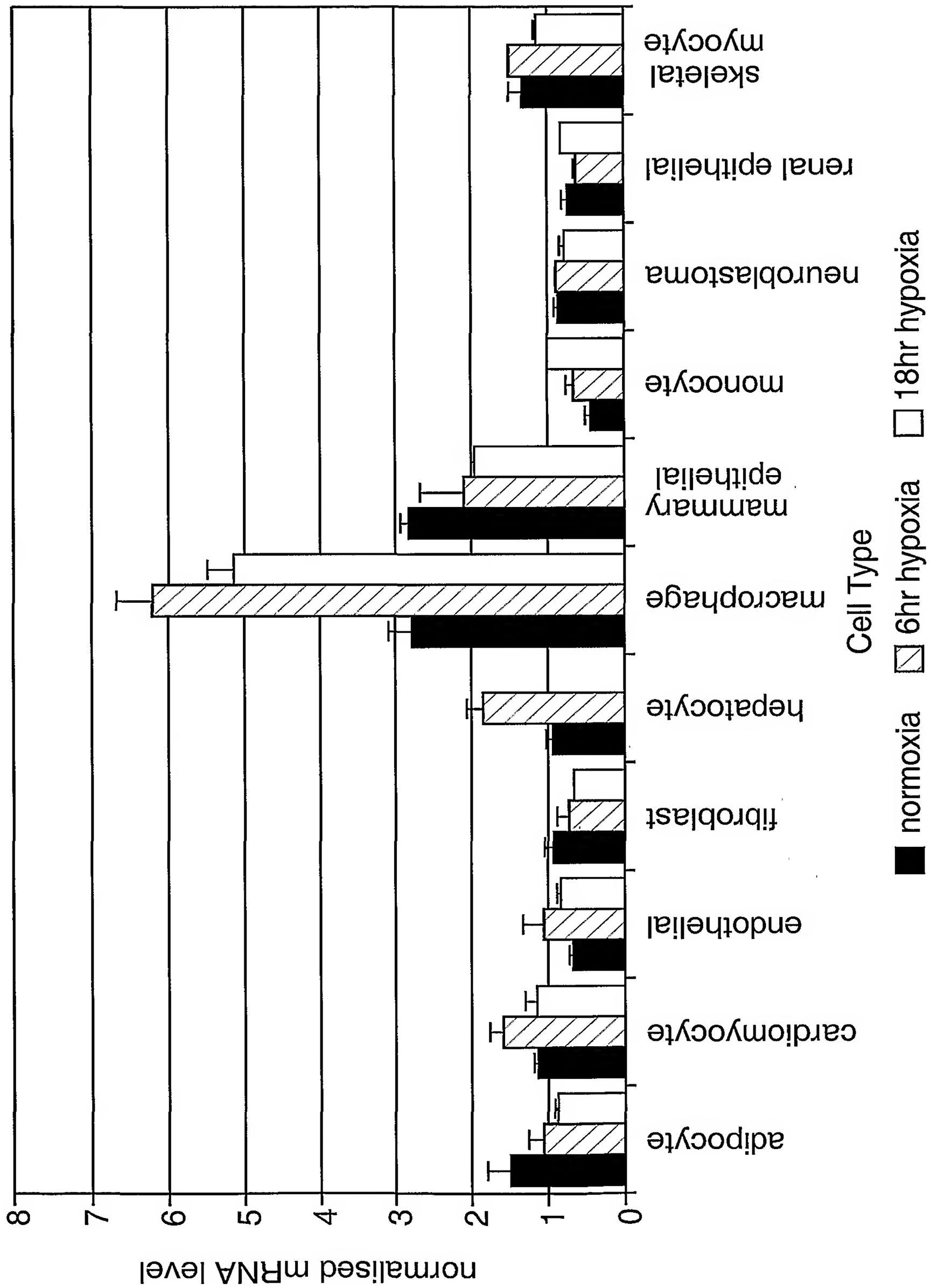


FIG .13 p1F4/ SeqID:340/ CYP1



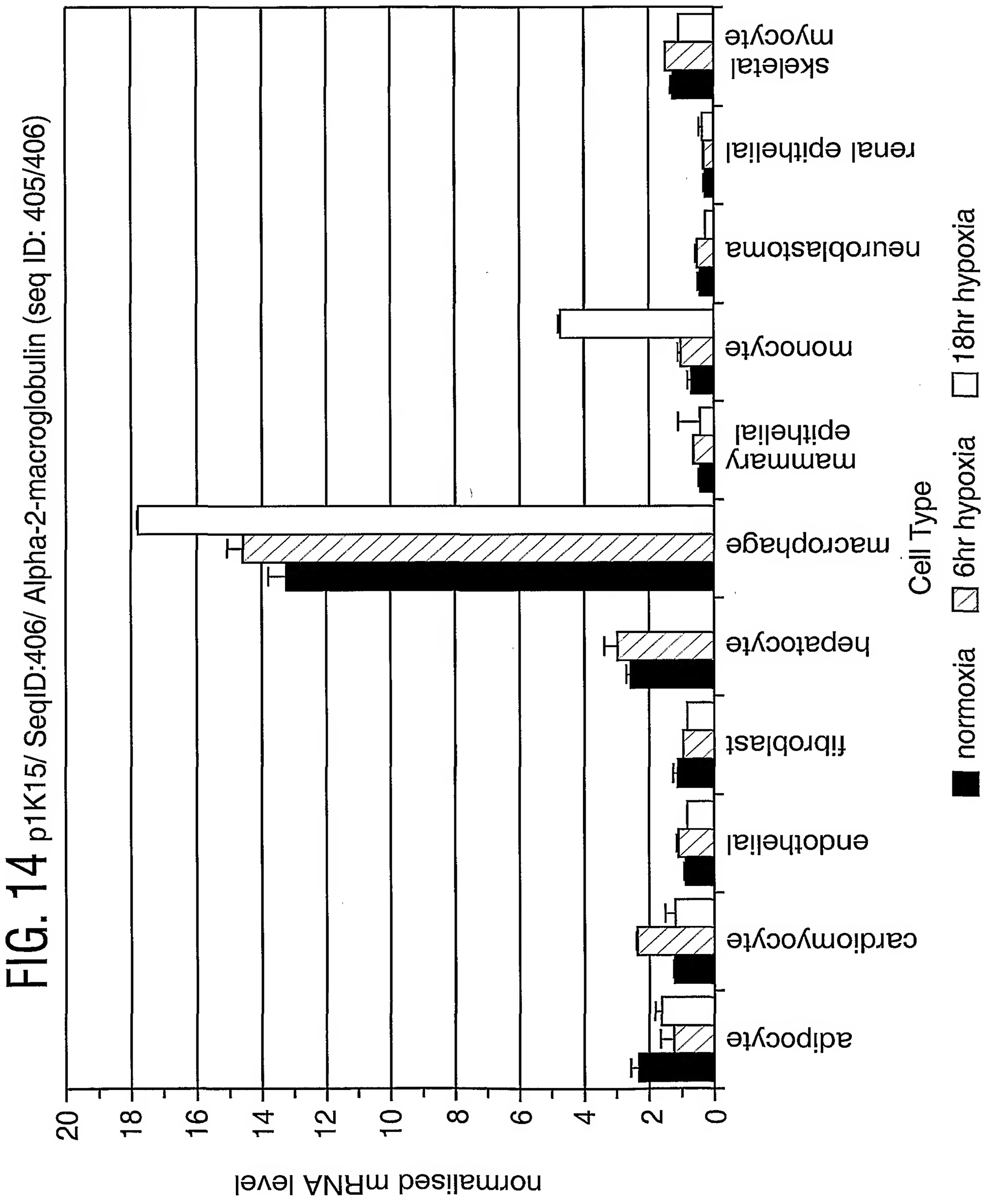

normalised mRNA level
0
2
4
6
8
10
12
14
16
18
20
adipocyte
cardiomyocyte
endothelial
fibroblast
hepatocyte
macrophage
mammary epithelial
monocyte
neuroblastoma
renal epithelial
skeletal myocyte
Cell Type
normoxia
6hr hypoxia
18hr hypoxia
p1K15/ SeqID:406/ Alpha-2-macroglobulin (seq ID: 405/406)

FIG. 14

FIG. 15 p1B23/ SeqID:358/ interleukin 1 receptor antagonist

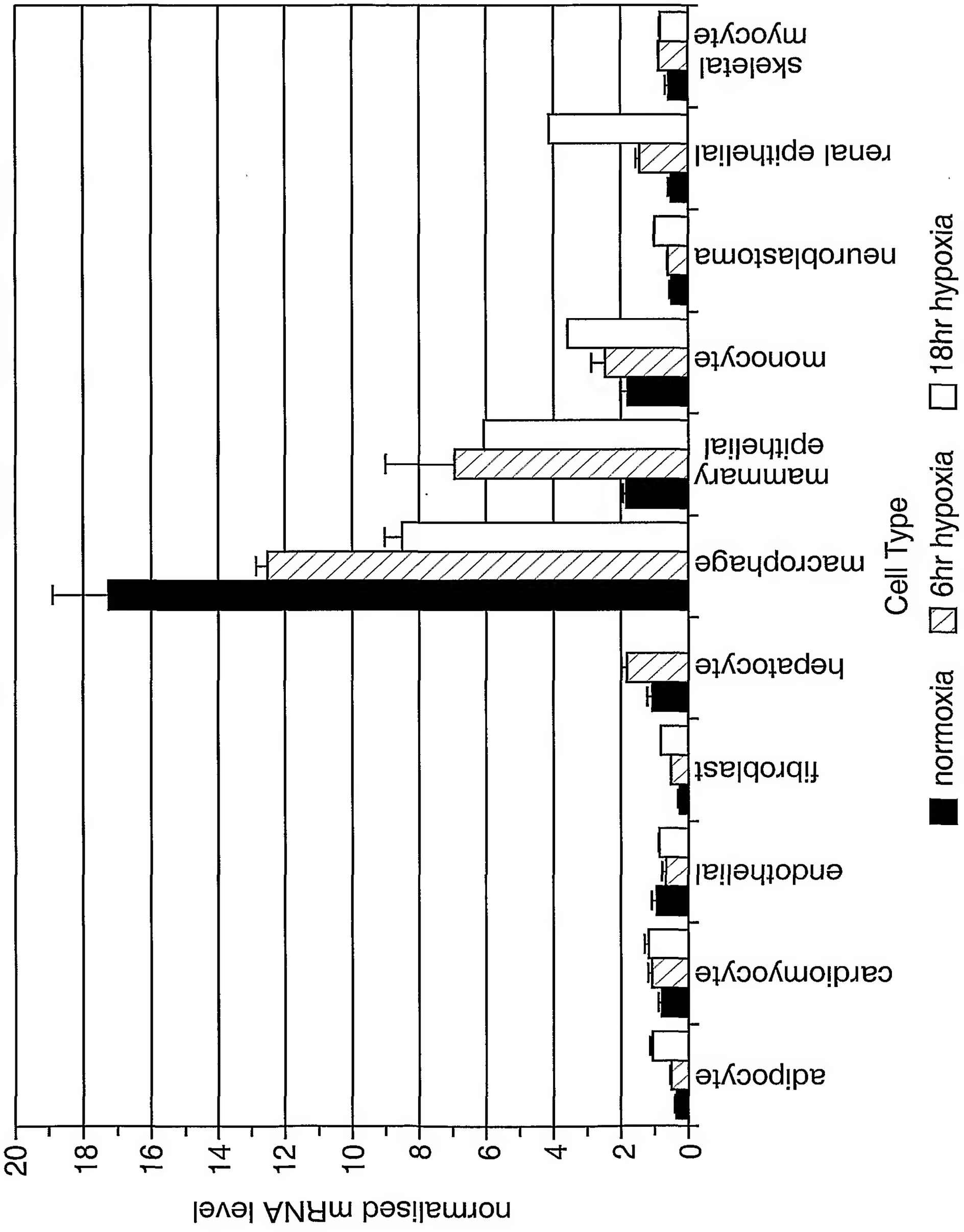
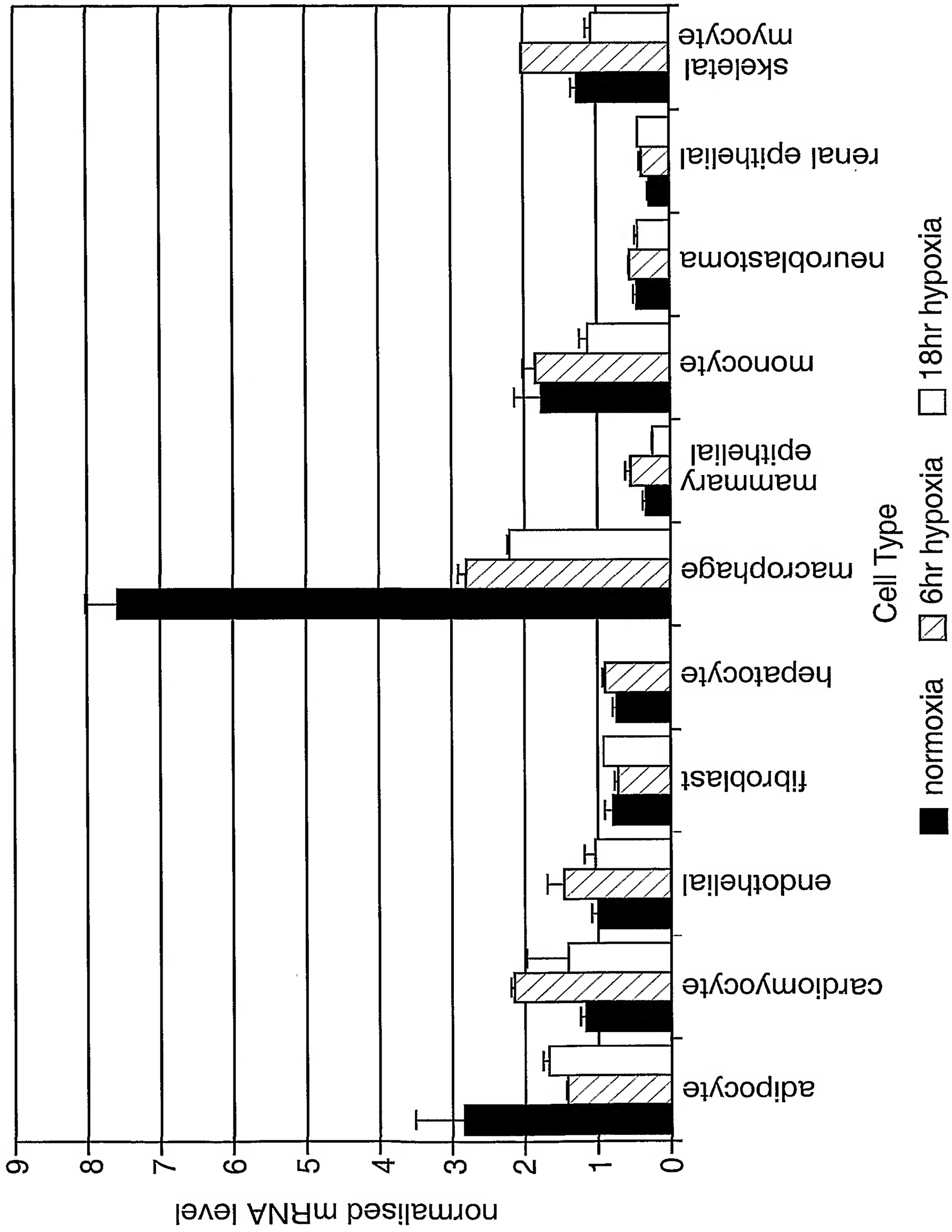


FIG. 16 p1I20/ SeqID:470/ SCYA3L



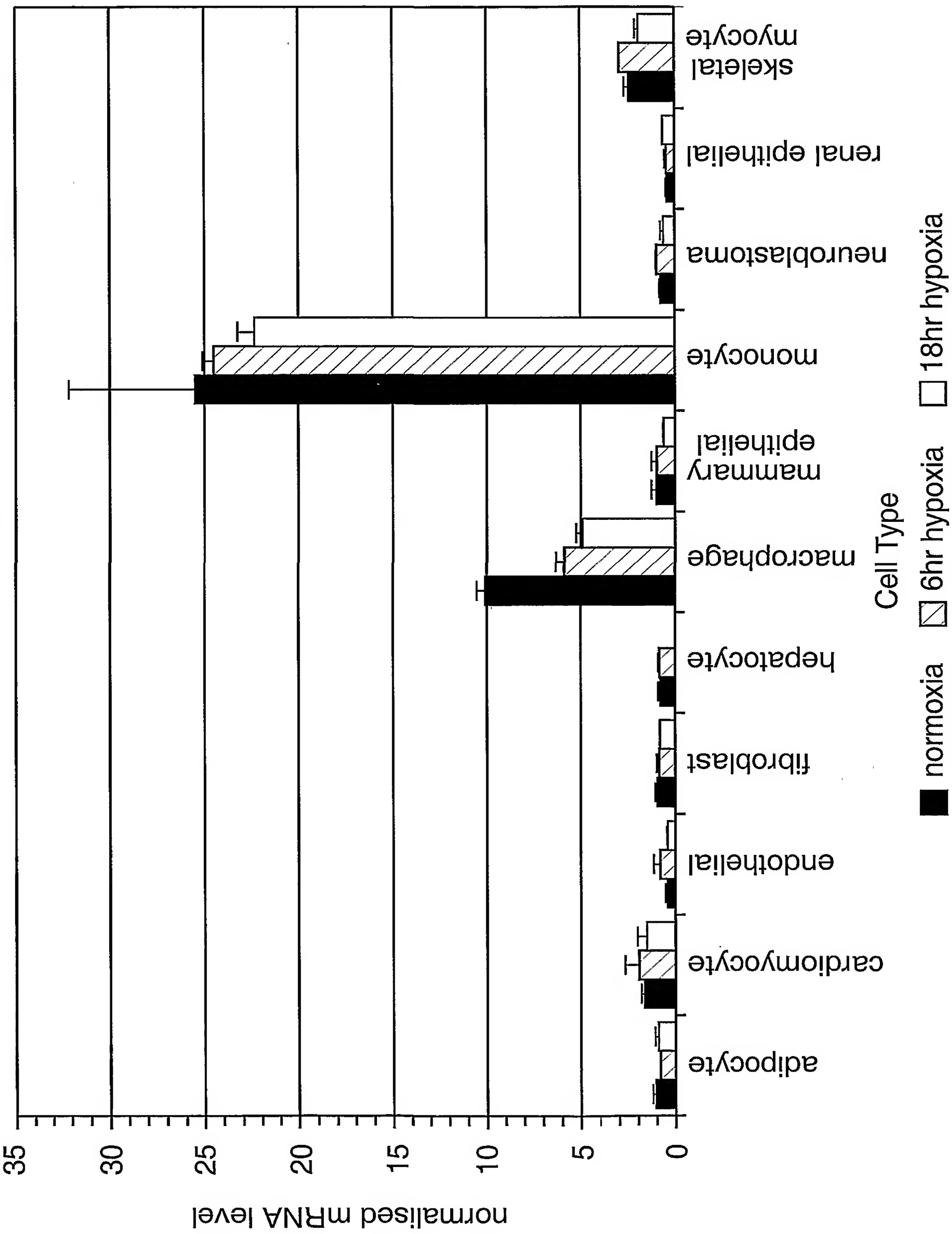
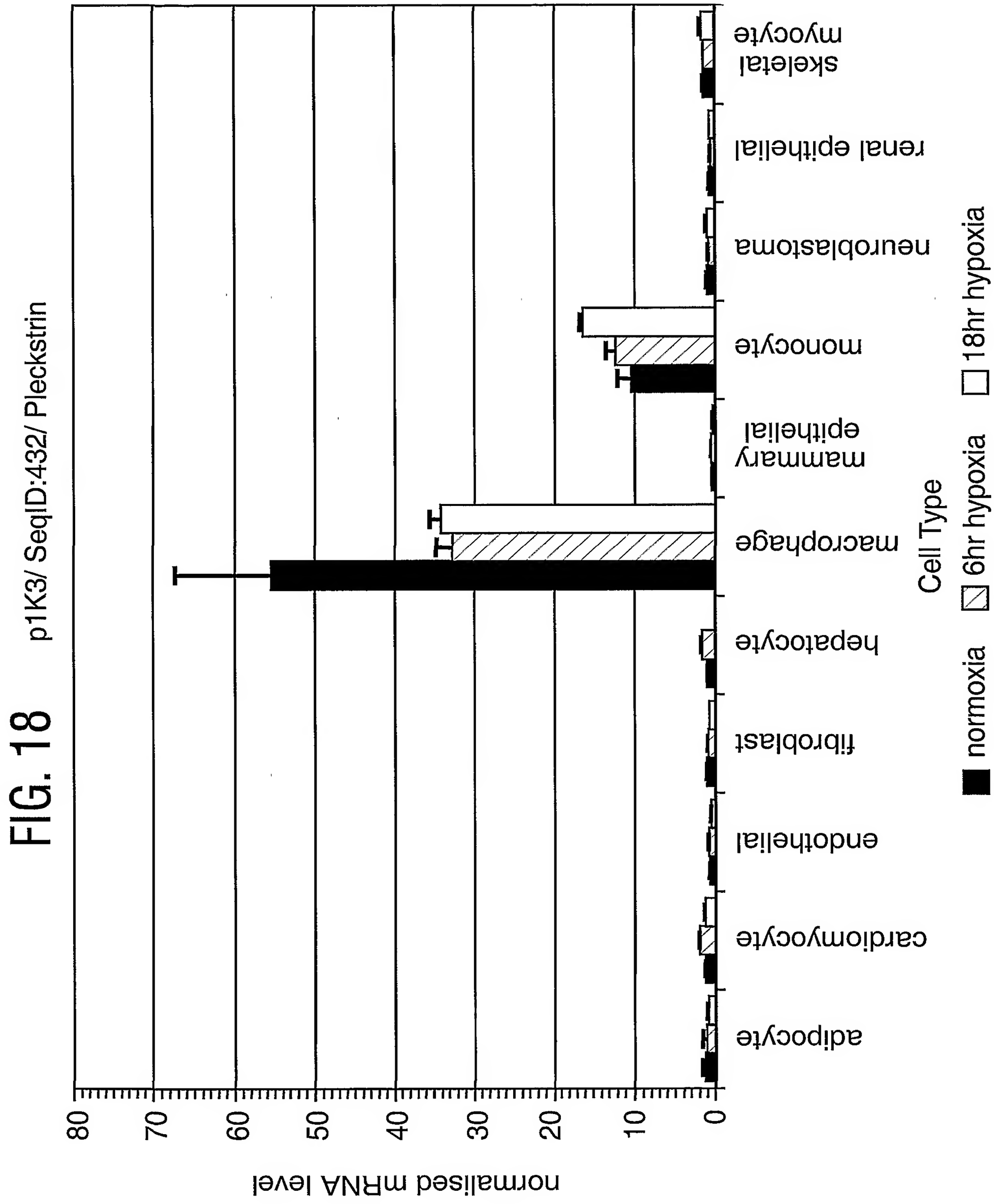


FIG. 17 p1K2/ SeqID:434/ CFFM4

FIG. 18 p1K3/ SeqID:432/ Pleckstrin



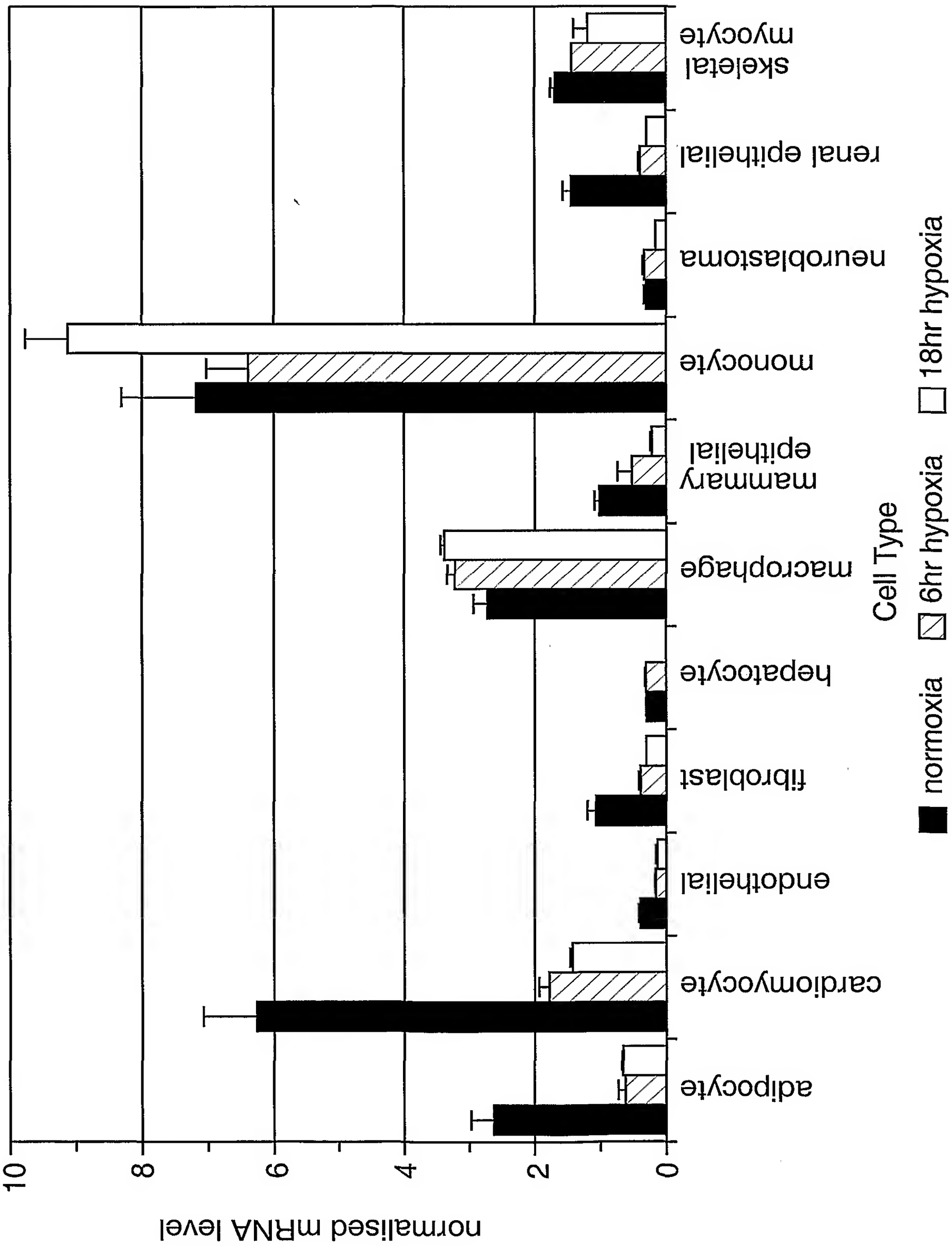


FIG. 19 p1F16/ SeqID:326/ CYP1B1

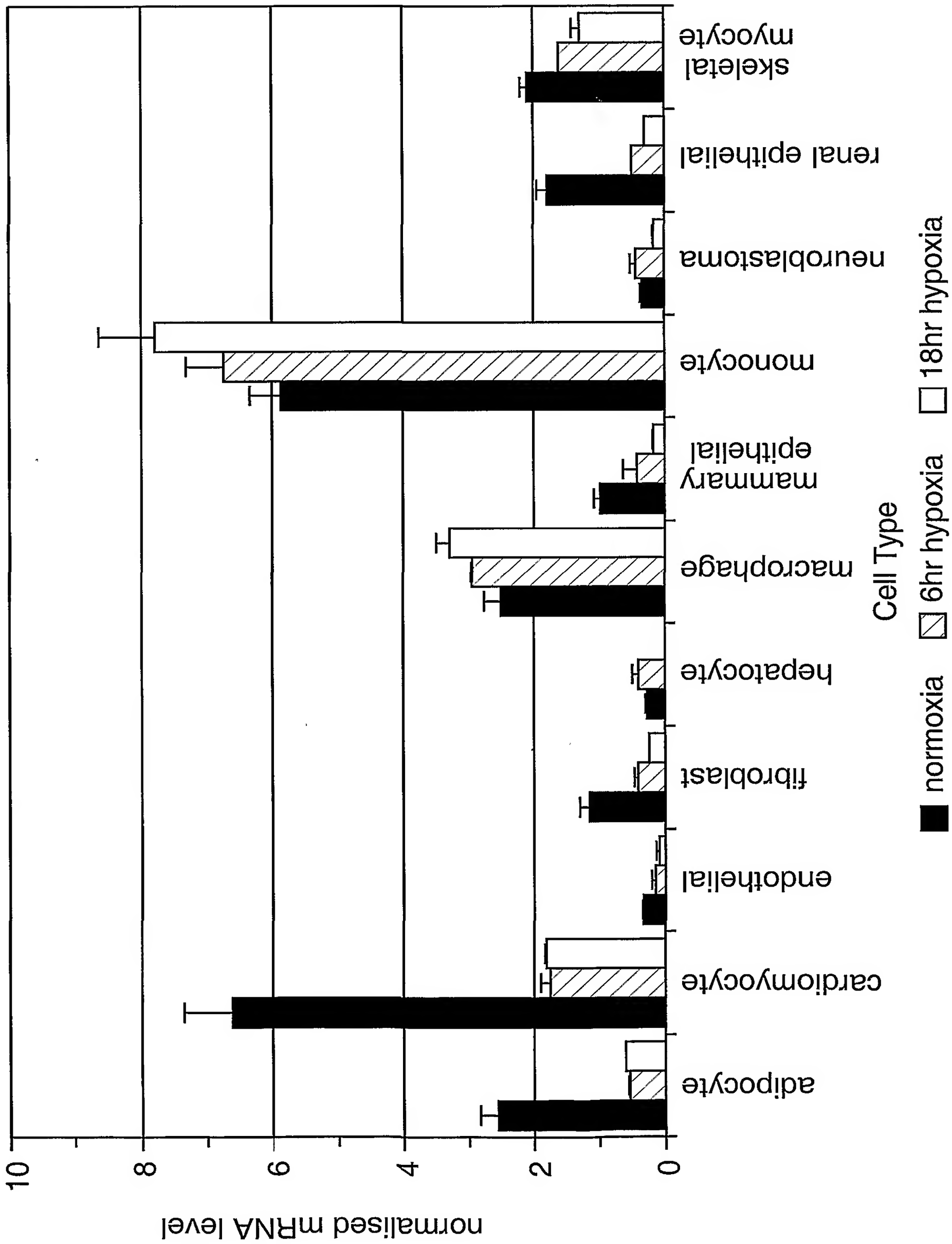


FIG. 20 p1E3/ SeqID:138/ CYP1B1

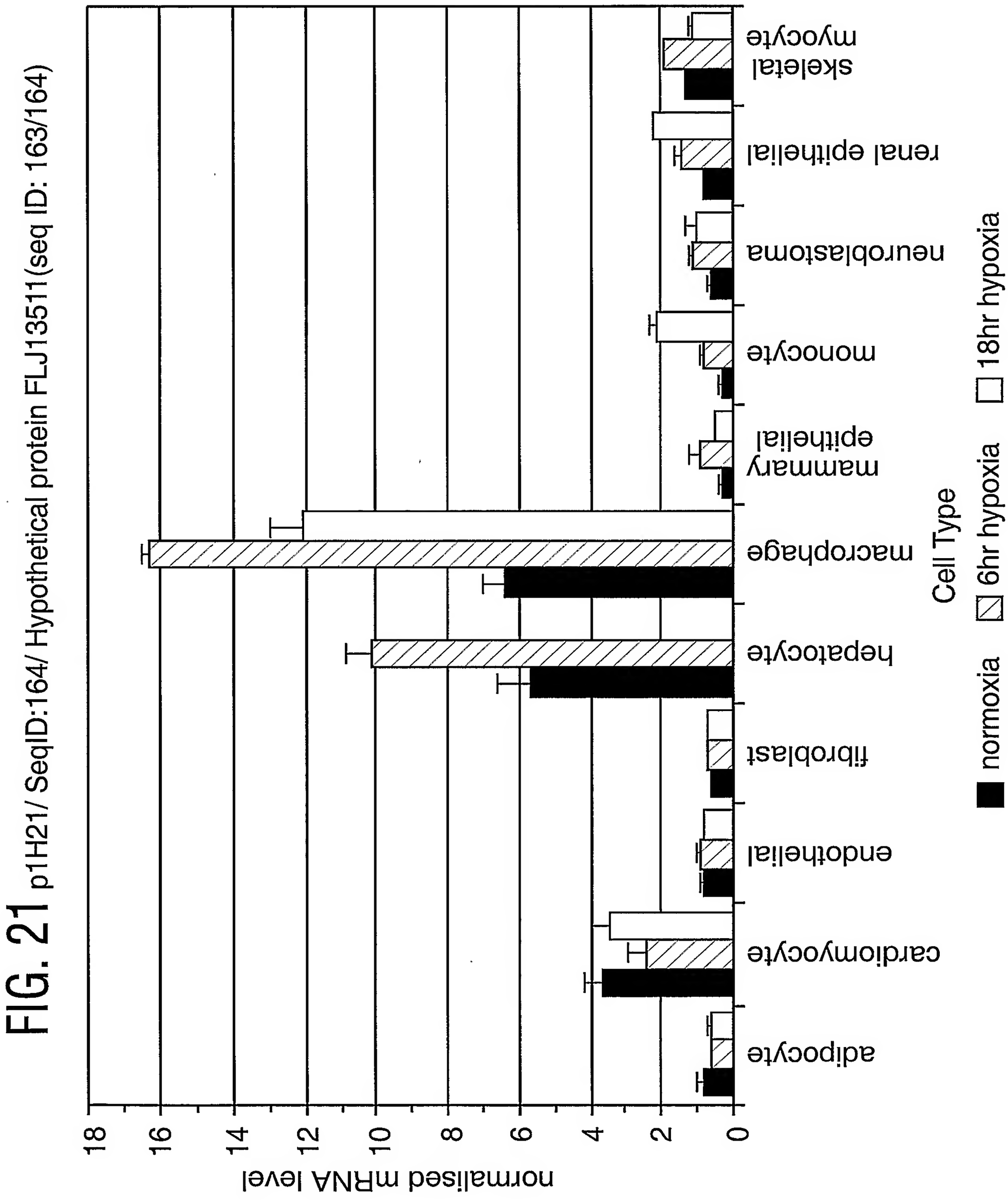

p1H21/ SeqID:164/ Hypothetical protein FLJ13511(seq ID: 163/164)
normalised mRNA level
0
2
4
6
8
10
12
14
16
18
Cell Type
normoxia
6hr hypoxia
18hr hypoxia
adipocyte
cardiomyocyte
endothelial
fibroblast
hepatocyte
macrophage
mammary epithelial
monocyte
neuroblastoma
renal epithelial
skeletal myocyte

FIG. 21

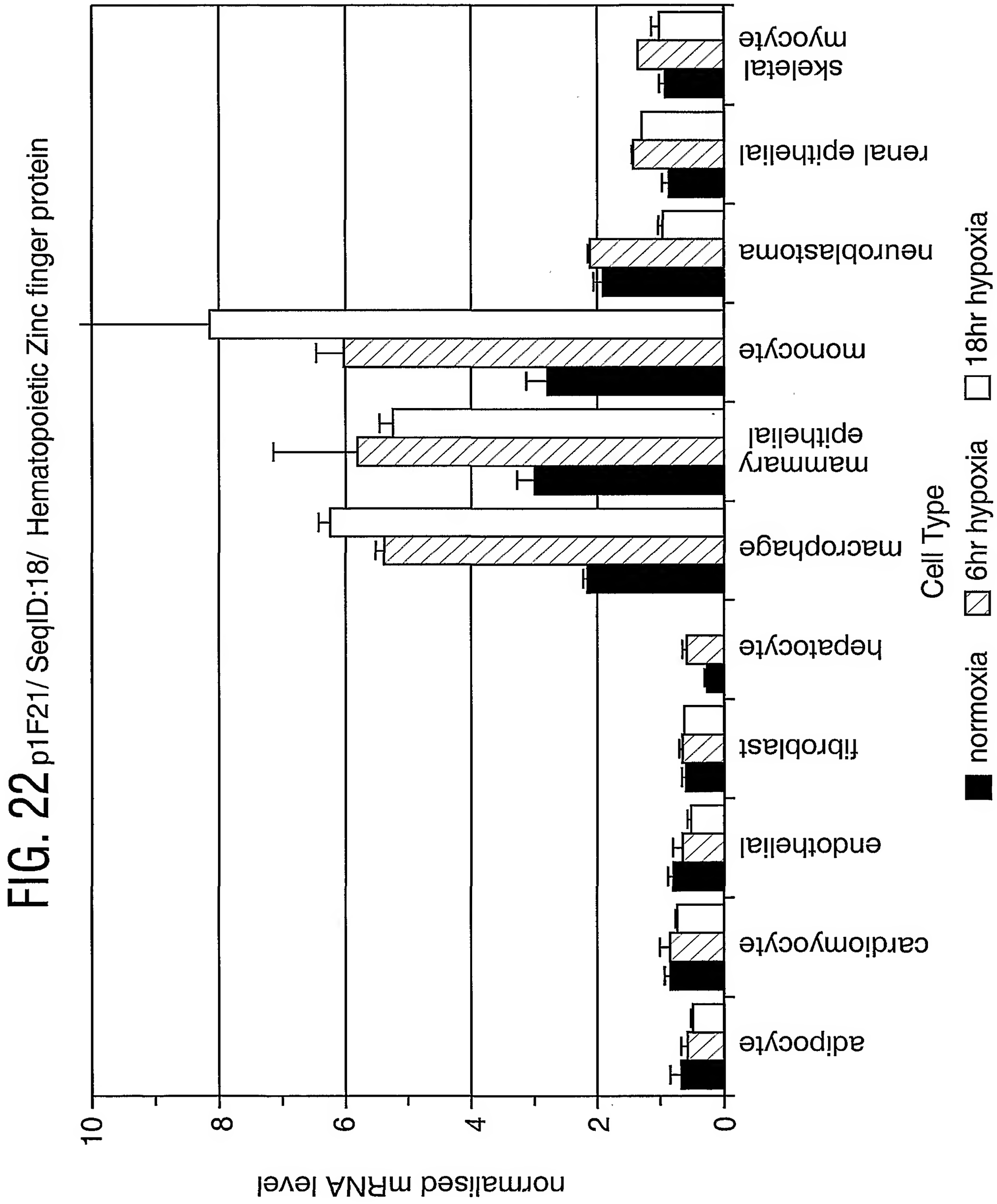
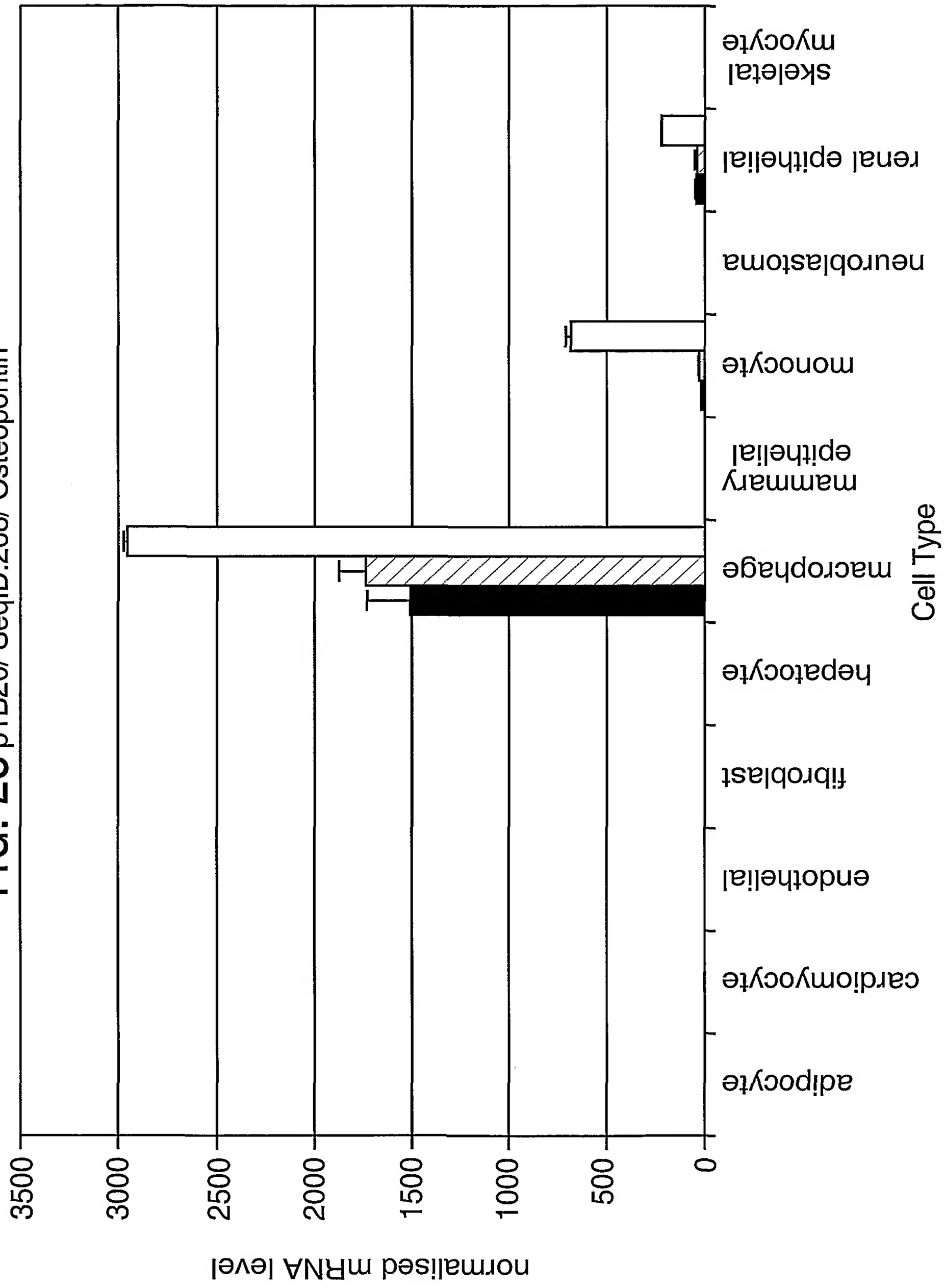


FIG. 22 p1F21/ SeqID:18/ Hematopoietic Zinc finger protein
normalised mRNA level
0
2
4
6
8
10
Cell Type
normoxia
6hr hypoxia
18hr hypoxia
adipocyte
cardiomyocyte
endothelial
fibroblast
hepatocyte
macrophage
mammary epithelial
monocyte
neuroblastoma
renal epithelial
skeletal myocyte

FIG. 23 p1B20/ SeqID:268/ Osteopontin



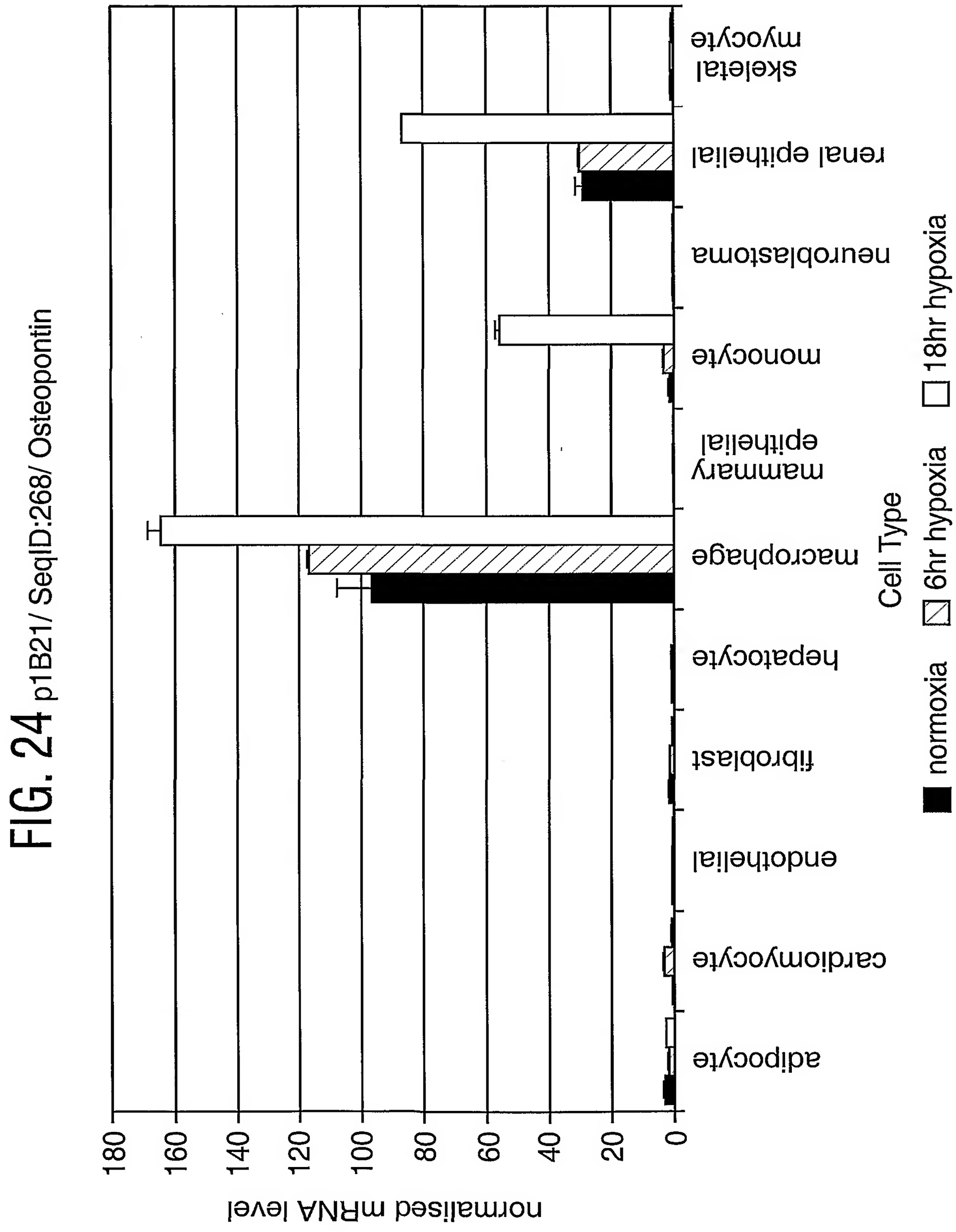


FIG. 24 p1B21/ SeqID:268/ Osteopontin
normalised mRNA level
0
20
40
60
80
100
120
140
160
180
adipocyte
cardiomyocyte
endothelial
fibroblast
hepatocyte
macrophage
mammary epithelial
monocyte
neuroblastoma
renal epithelial
skeletal myocyte
normoxia
6hr hypoxia
18hr hypoxia
Cell Type

FIG. 25 p1B9/ SeqID:314/ adipophilin

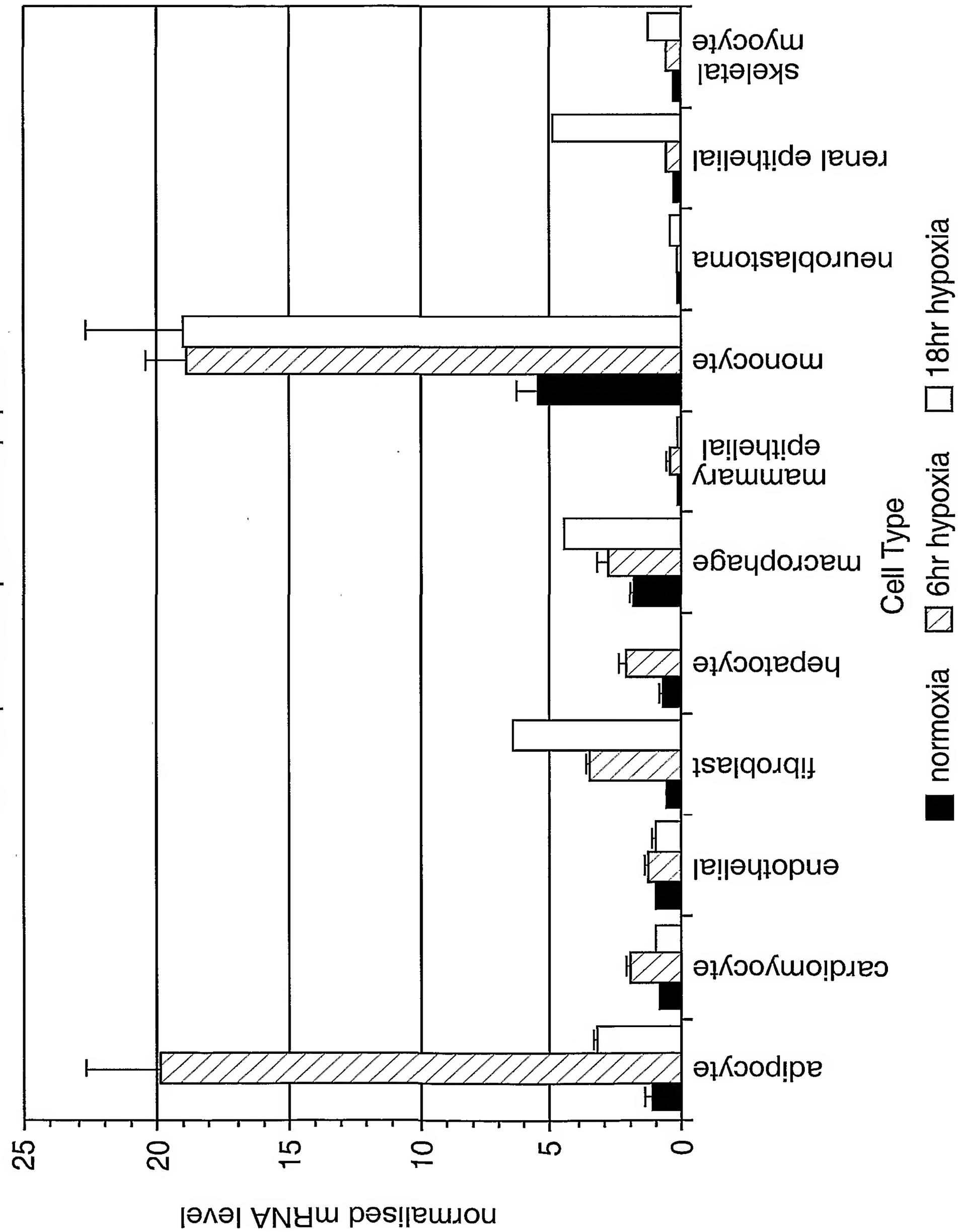


FIG. 26 p1B8/ SeqID:314/ adipophilin

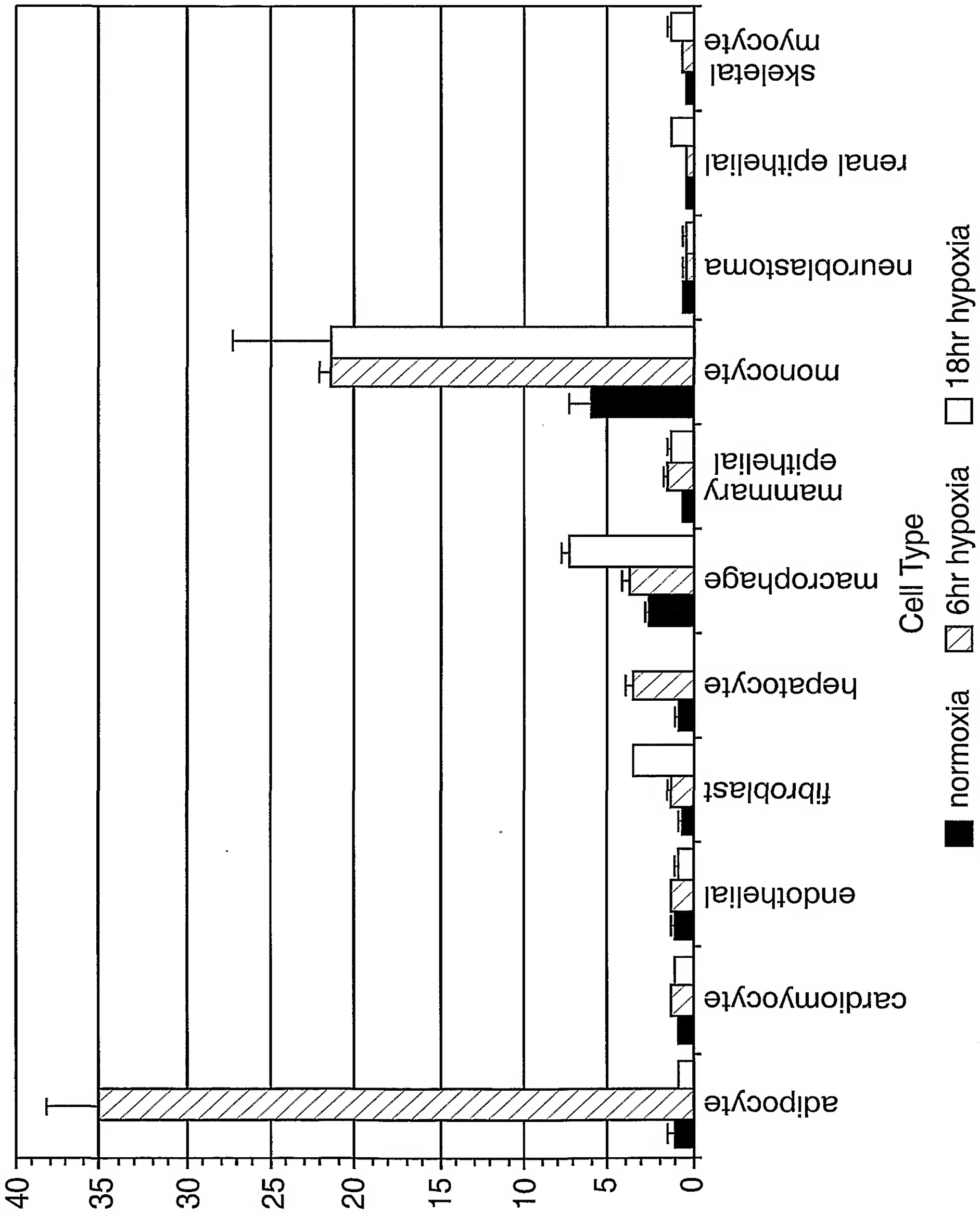


FIG. 27 p1B7/ SeqID:314/ adipophilin

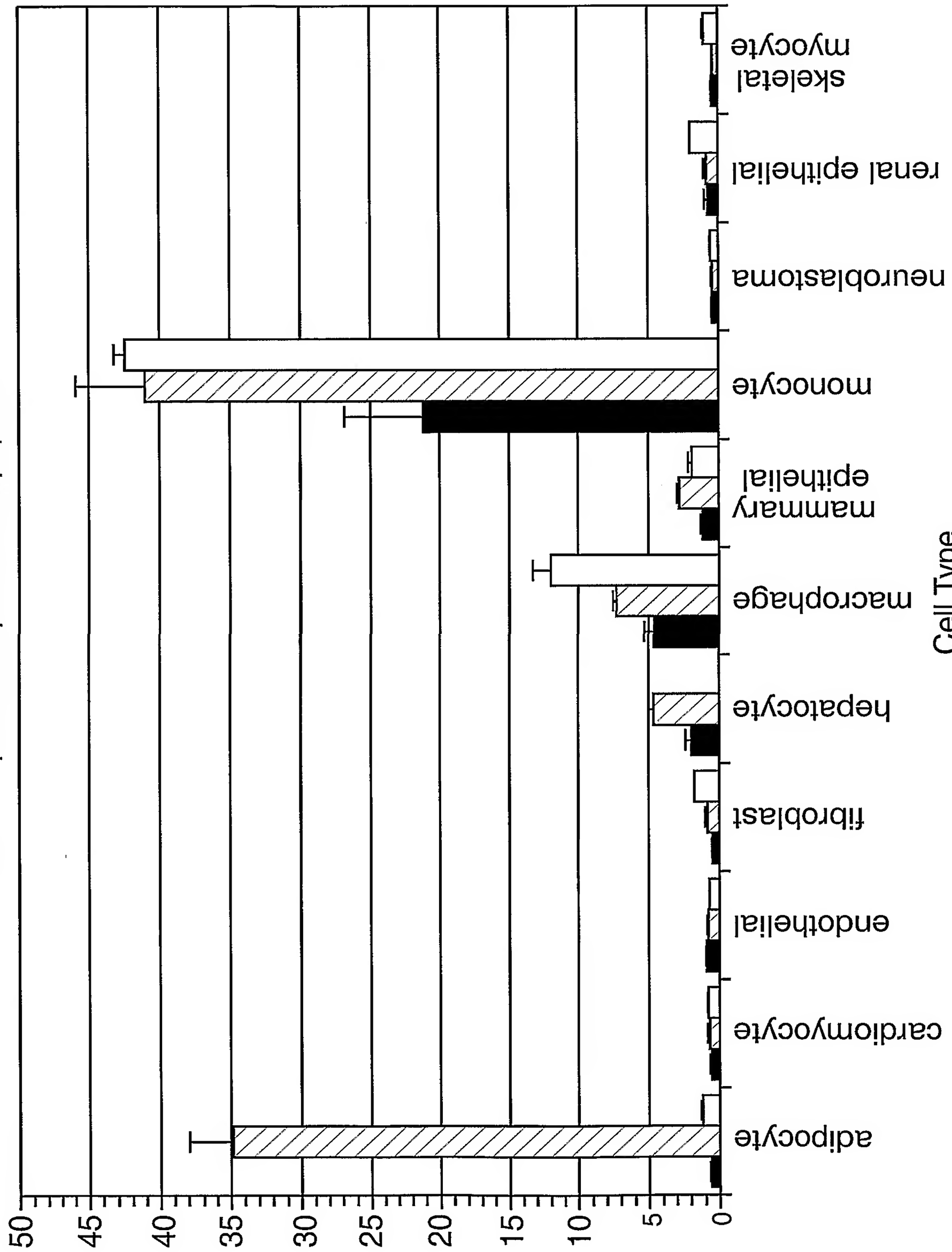


FIG. 28 p1B6/ SeqID:314/ adipophilin

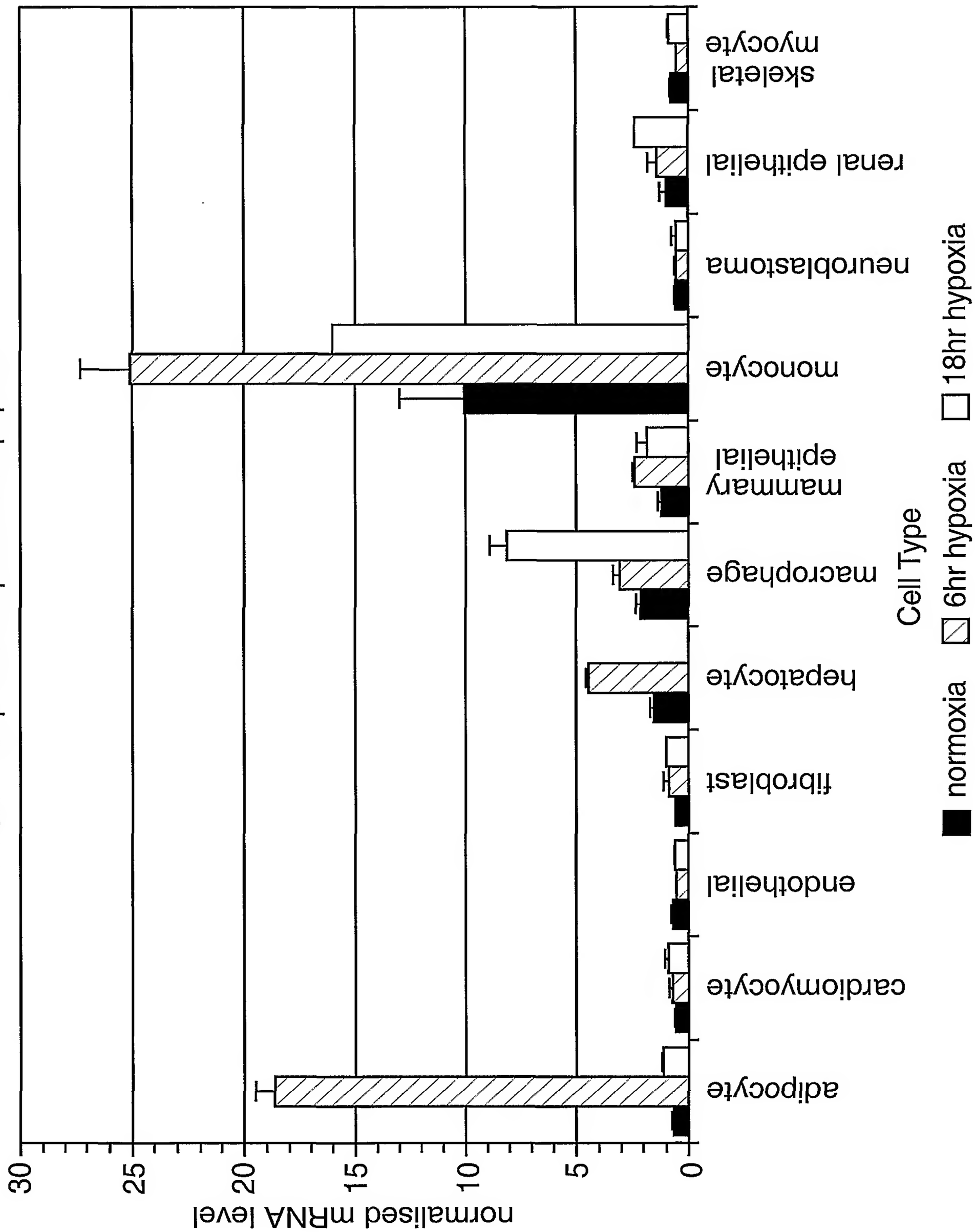


FIG. 29 p1H5/ SeqID:206/ Hypothetical protein FLJ22690

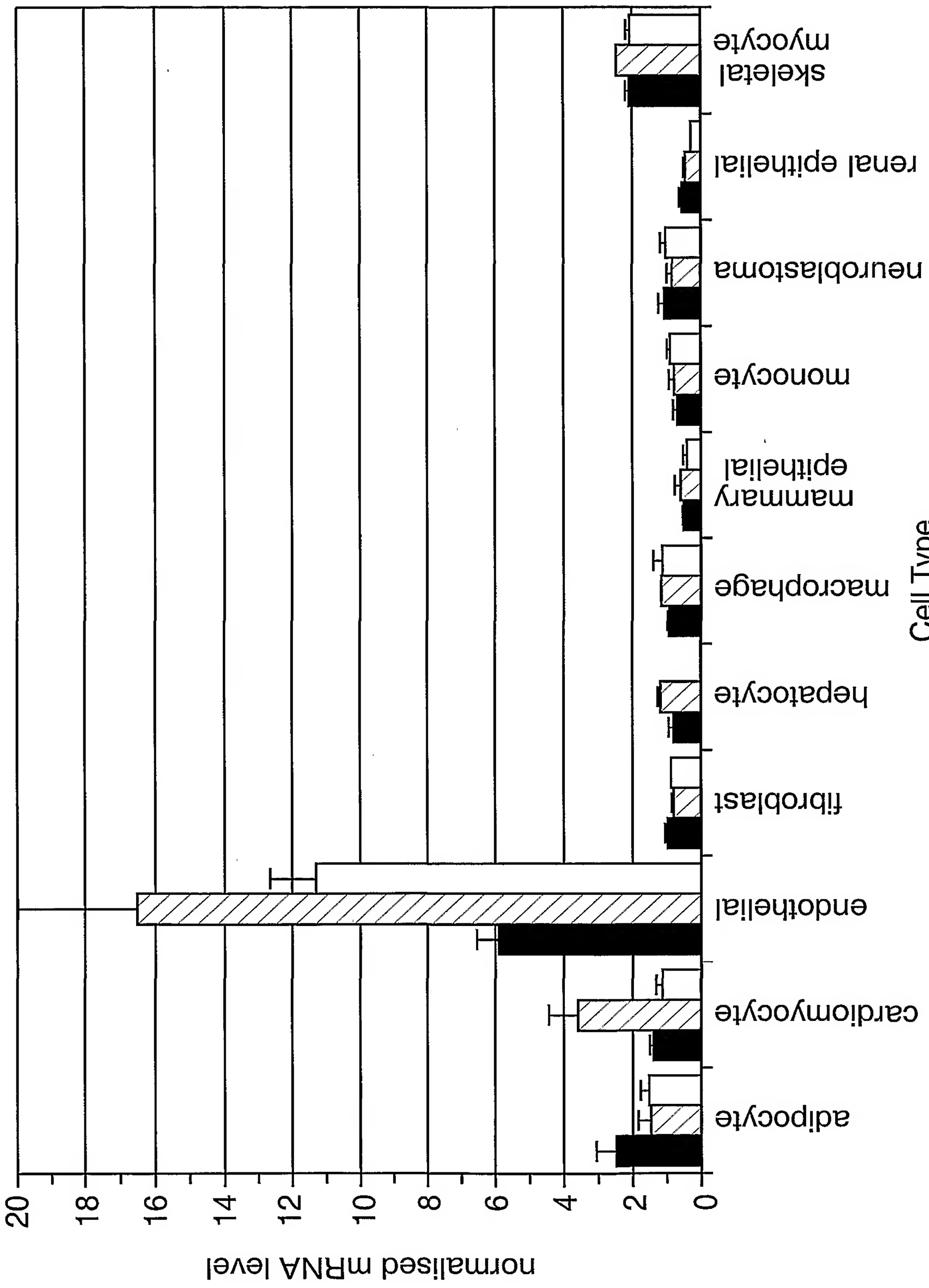


FIG. 30 p1E16/ SeqID:66/ cDNA DKFZp586E1624

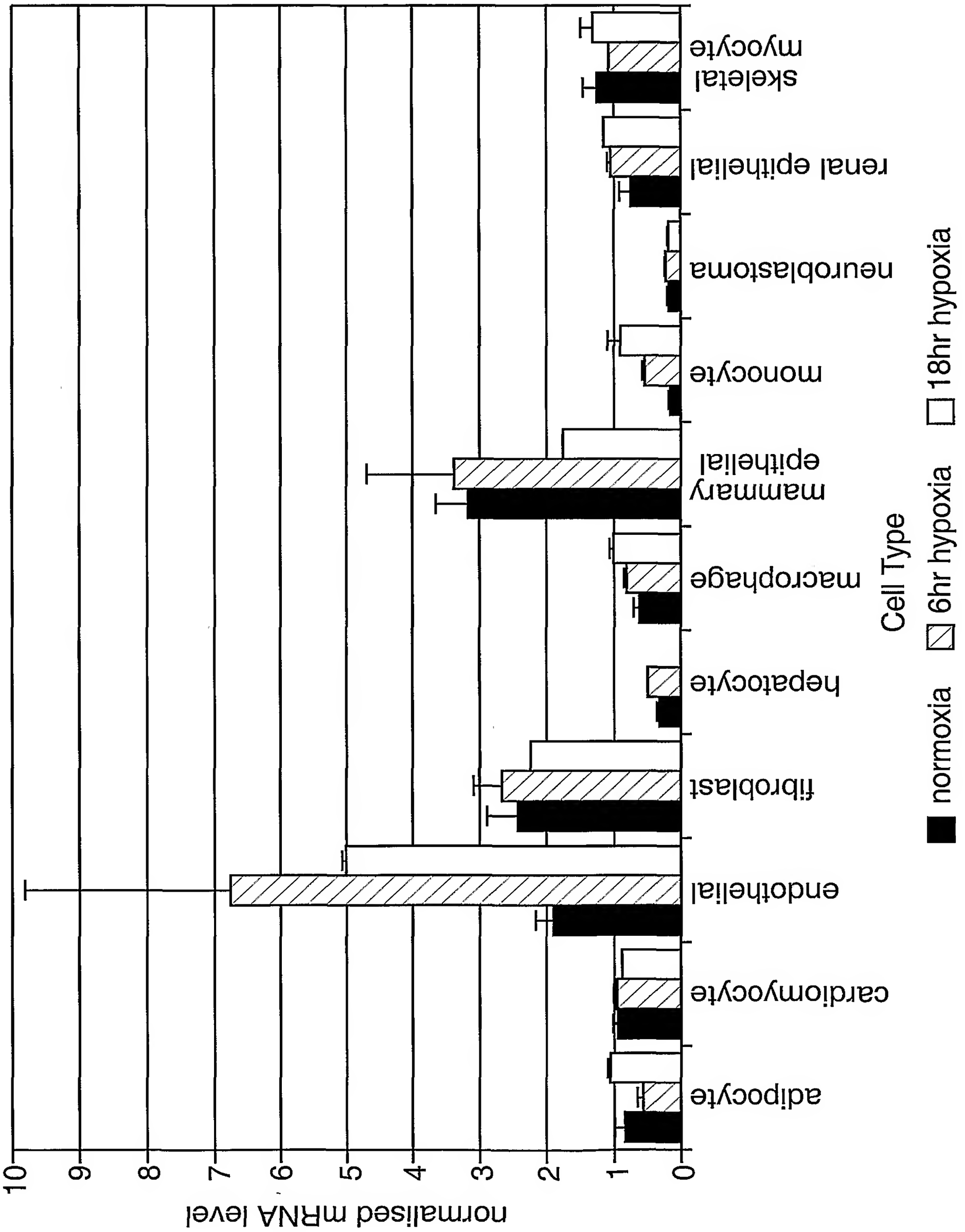


FIG. 31 p1G22/ SeqID:198/ EST

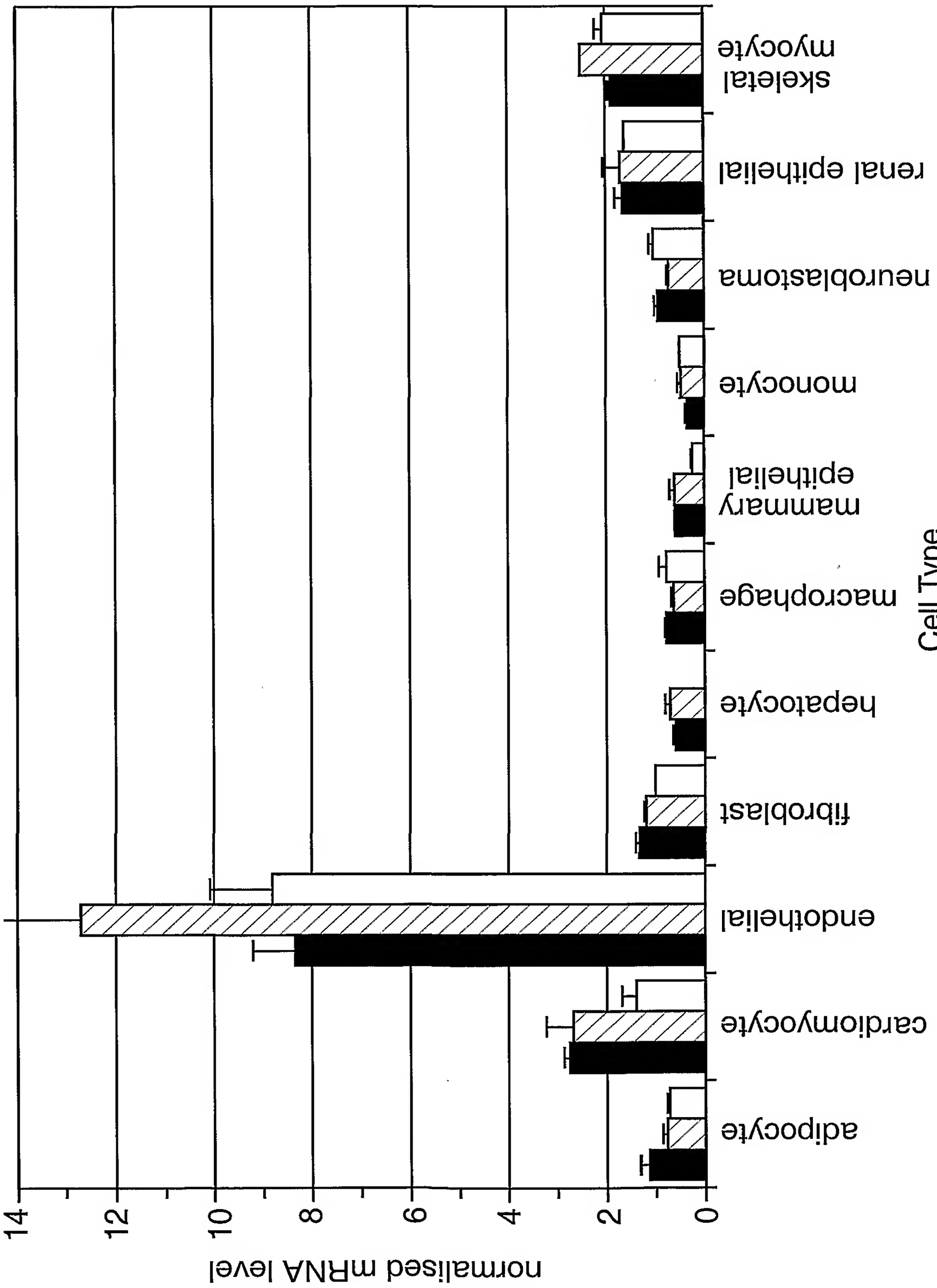


FIG. 32a p1E6/ SeqID:86/ EGL nine (C.elegans) homolog 3

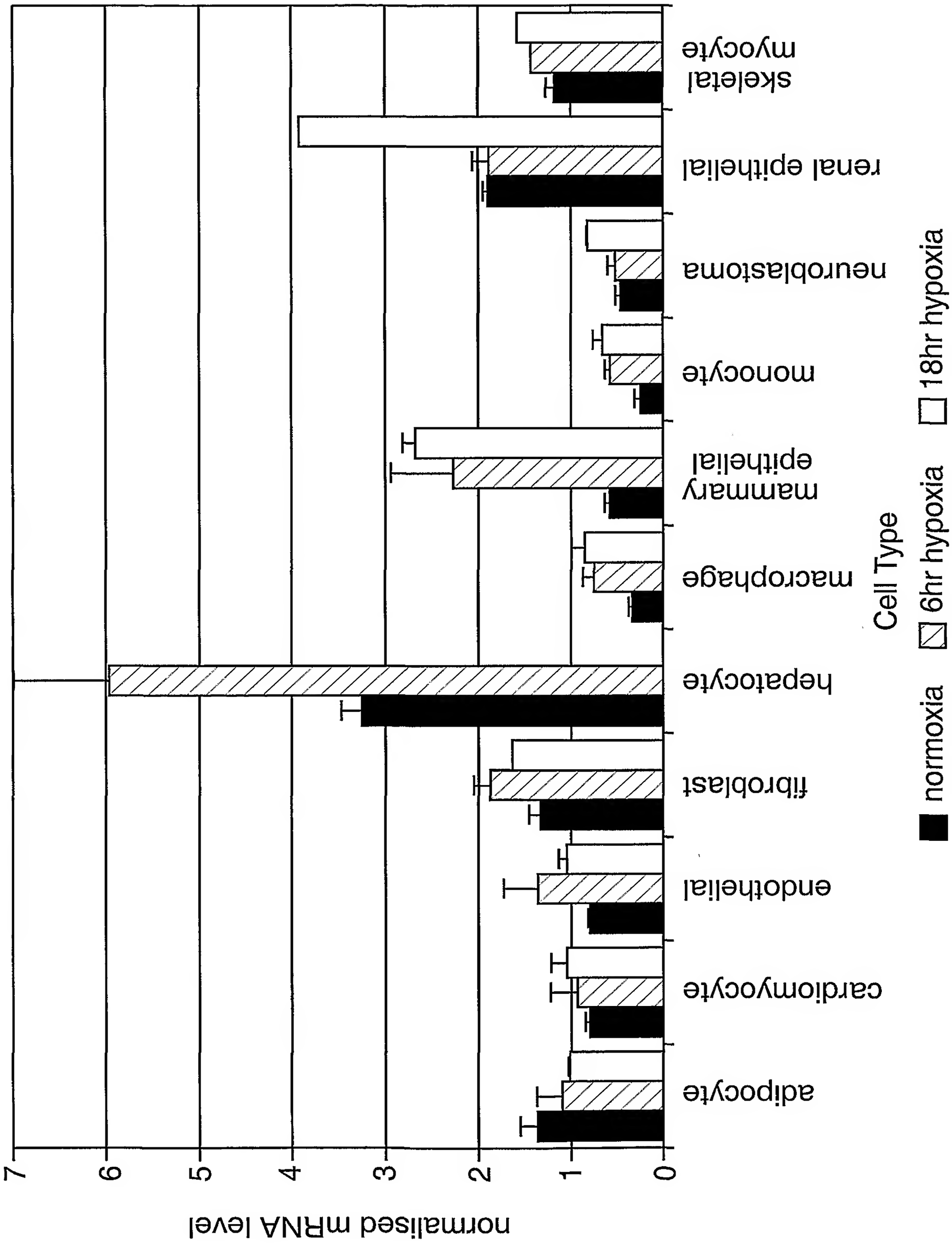


FIG. 32c

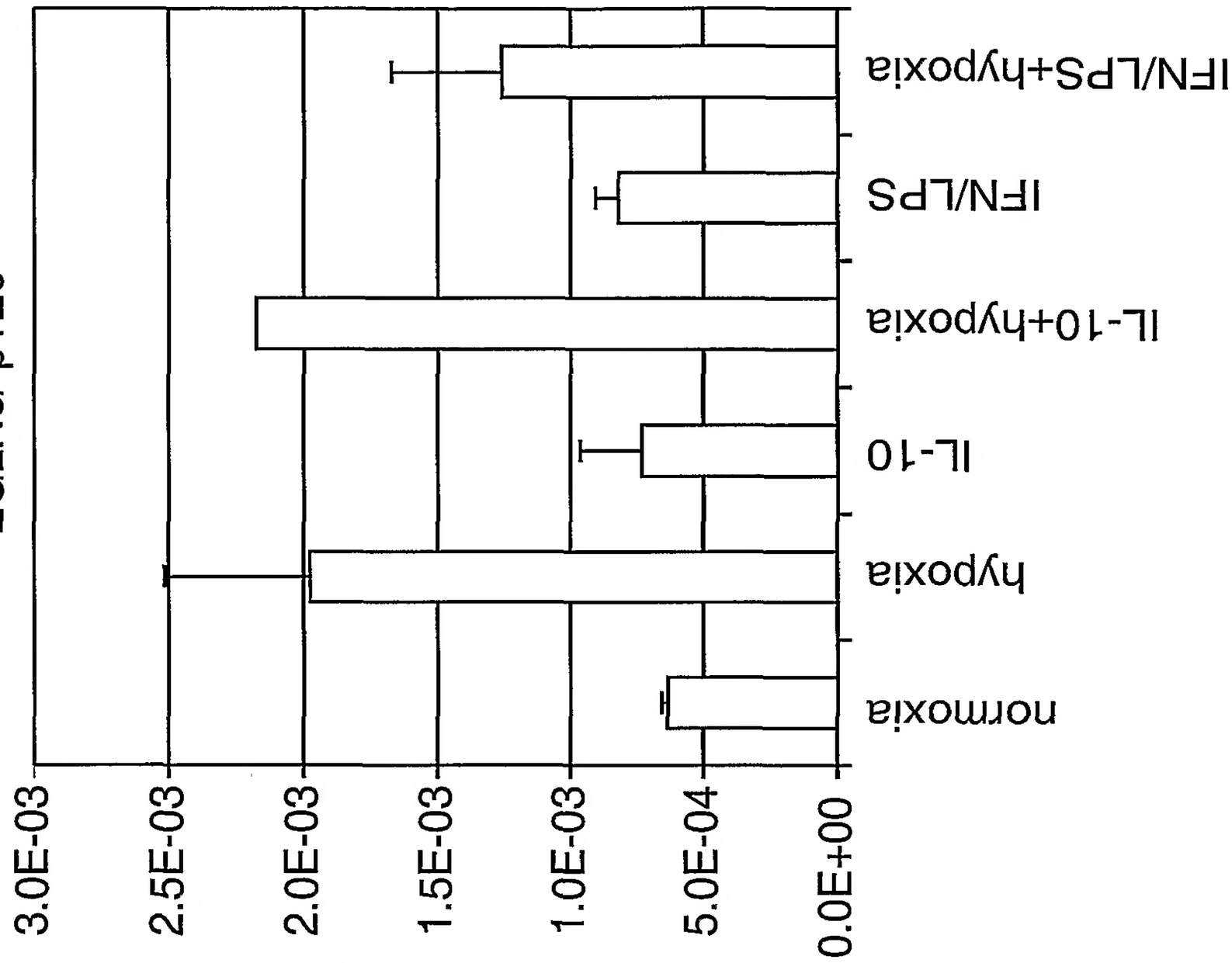


FIG. 32b

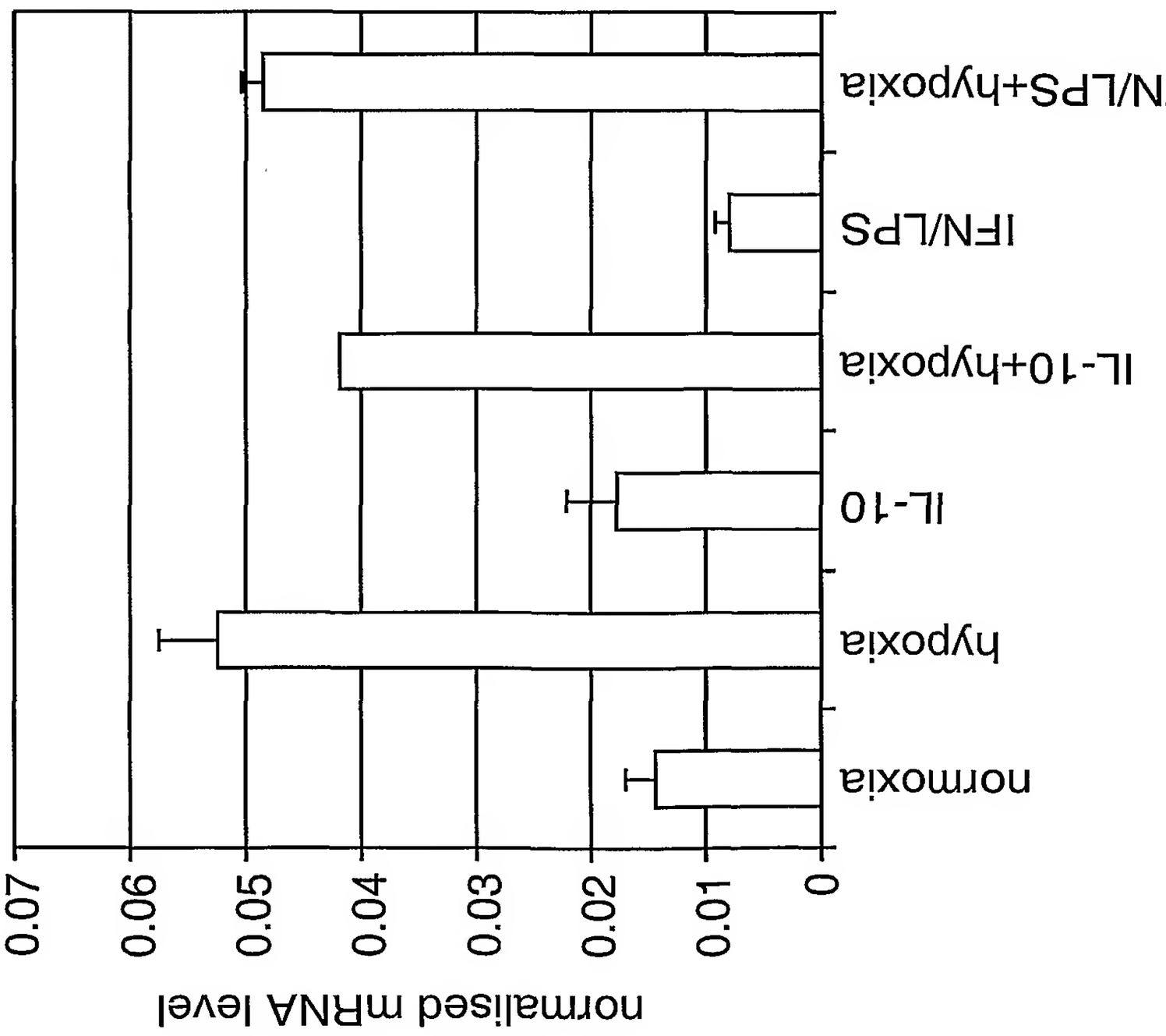


FIG. 32d p1D14/ C1orf12

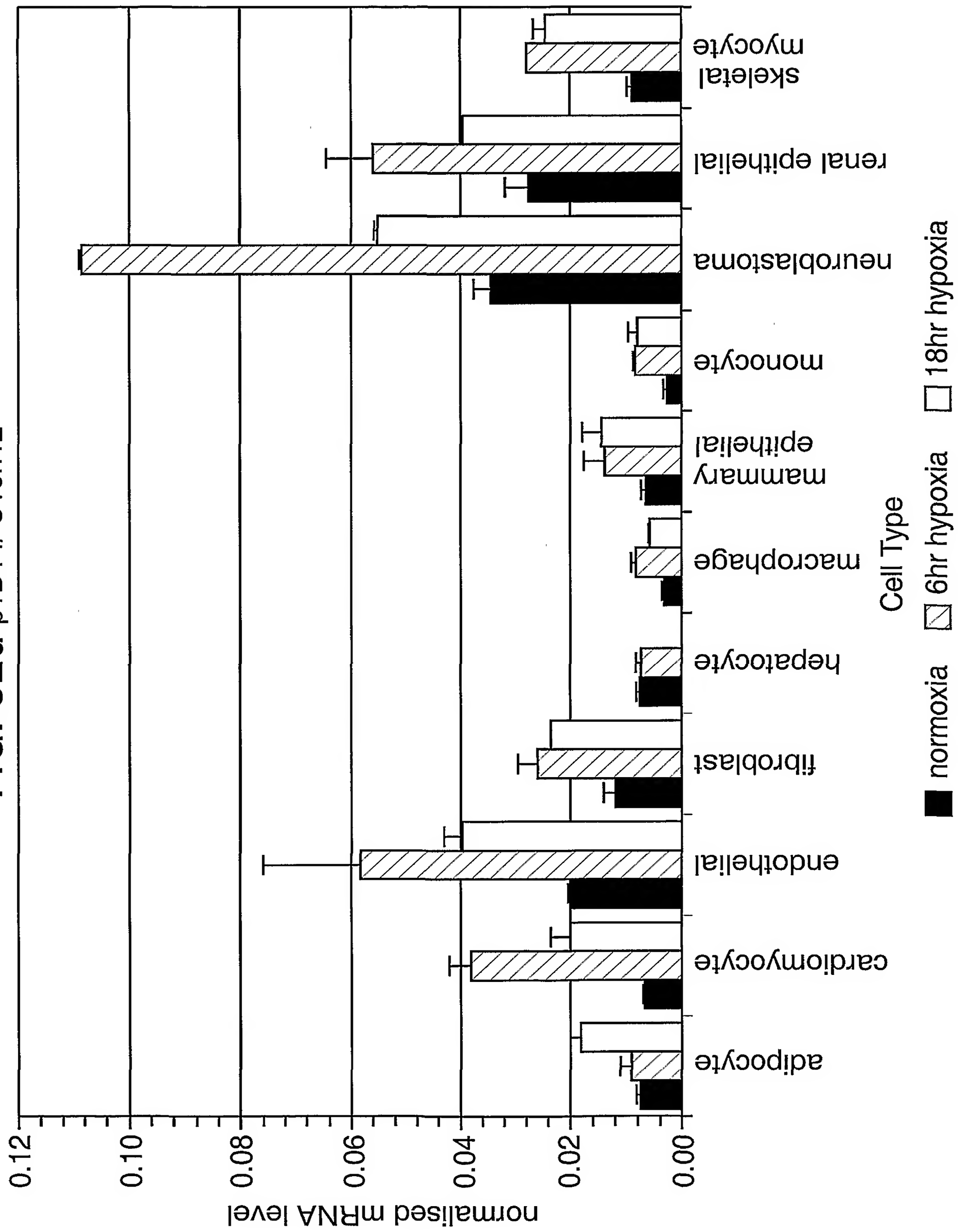


FIG. 32e

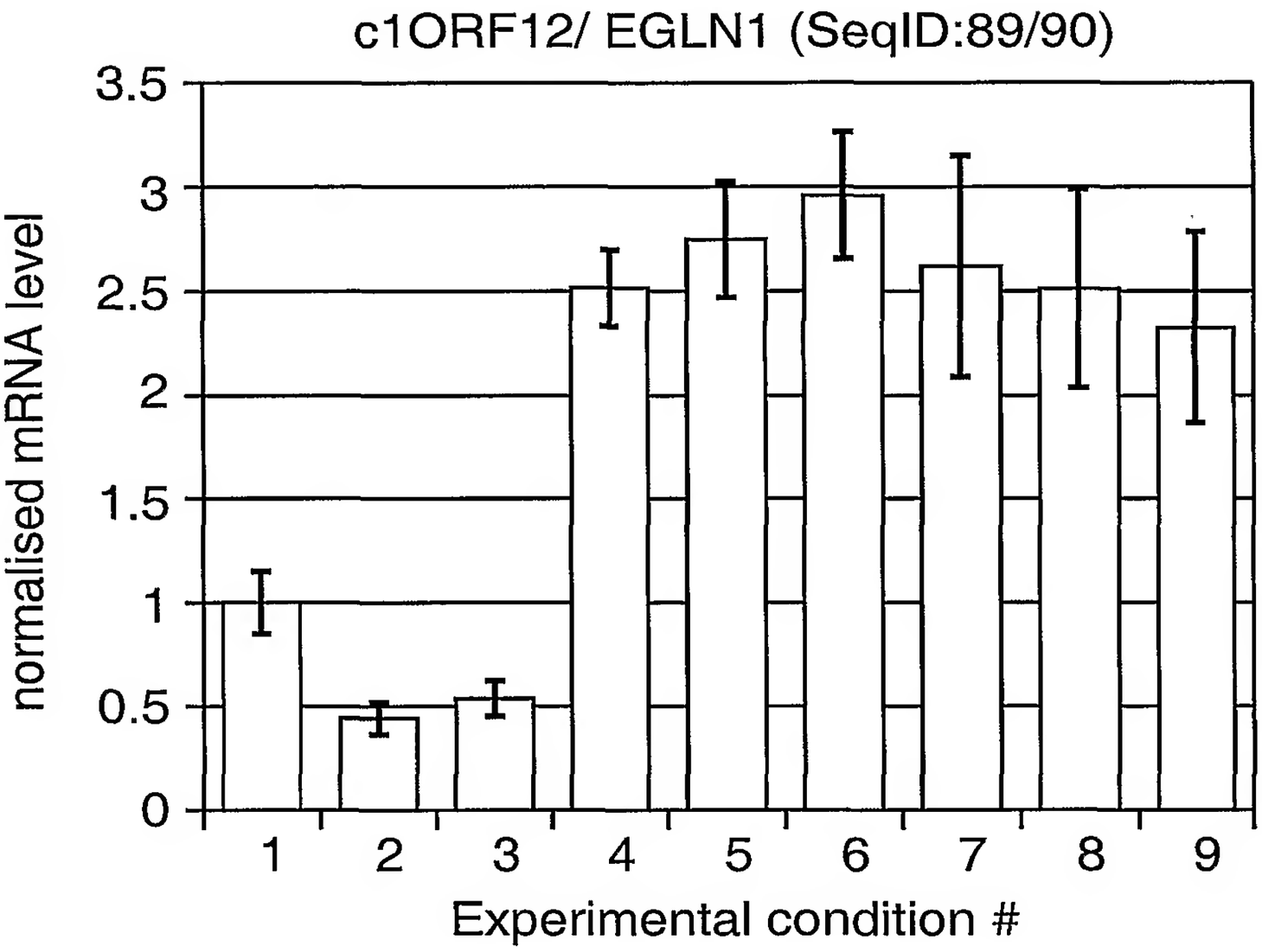


FIG. 32f

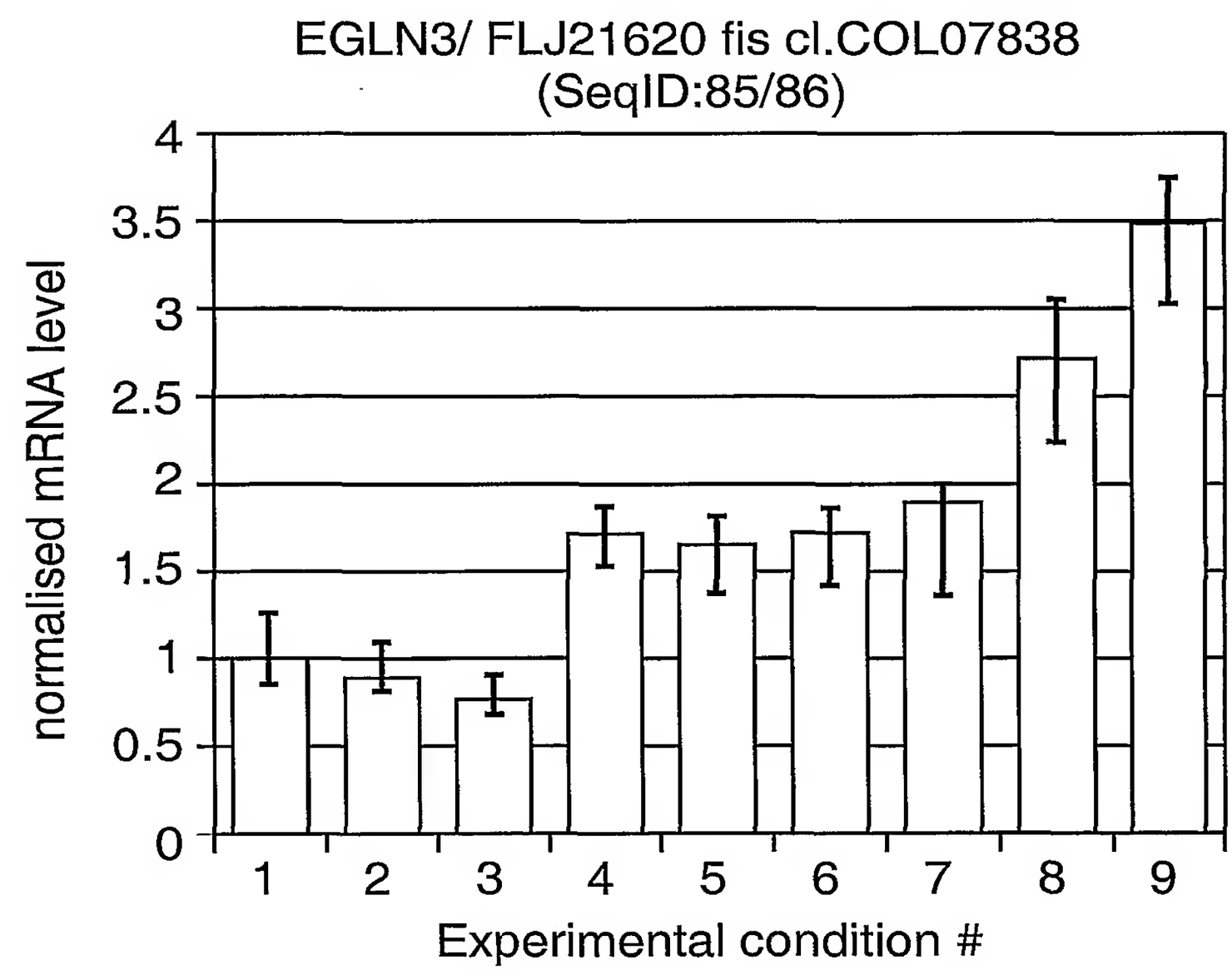


FIG. 32g

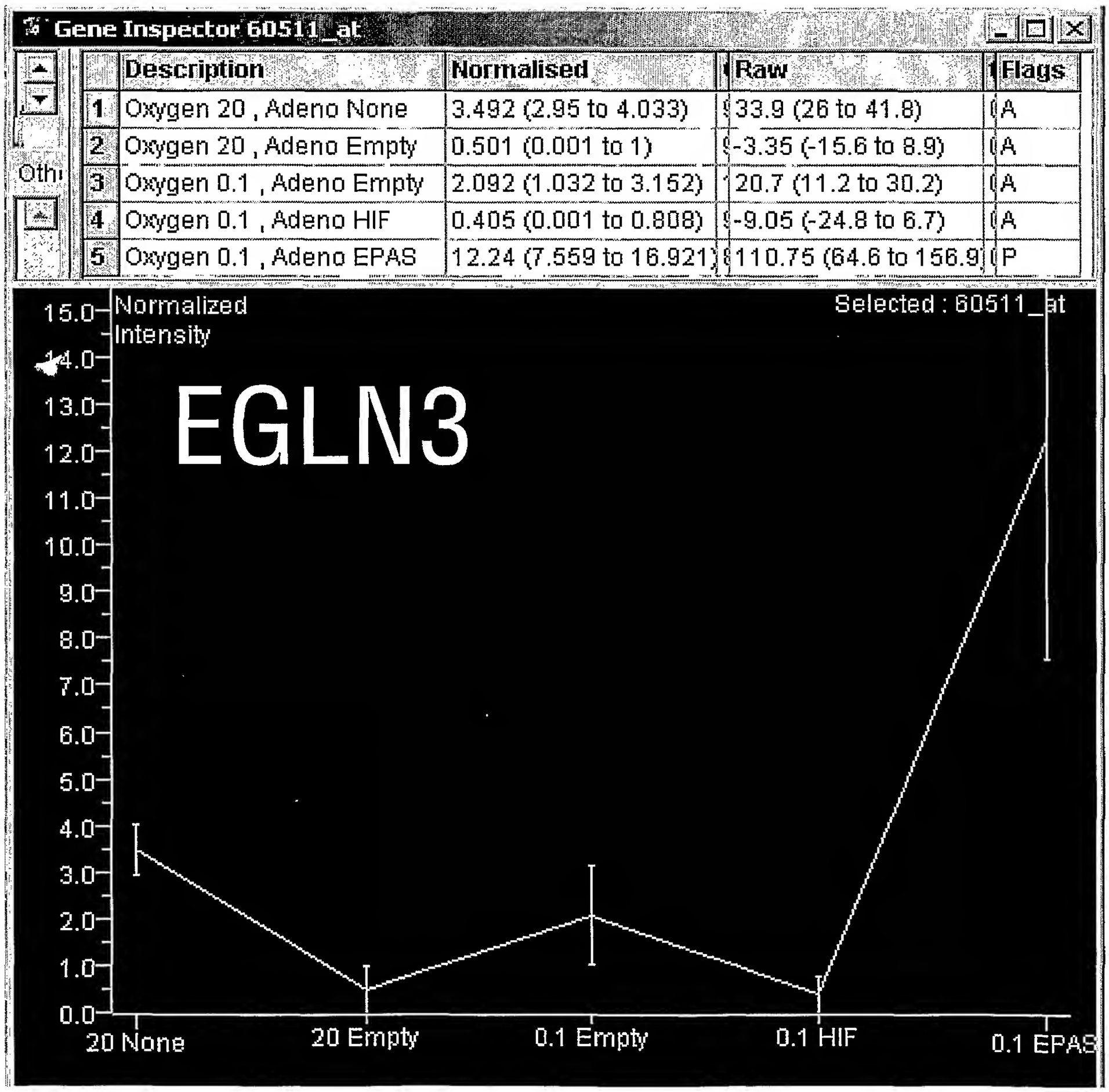

Gene Inspector 60511_at
Description
Normalised
Raw
Flags
1 Oxygen 20 , Adeno None 3.492 (2.95 to 4.033) 33.9 (26 to 41.8) A
2 Oxygen 20 , Adeno Empty 0.501 (0.001 to 1) -3.35 (-15.6 to 8.9) A
3 Oxygen 0.1 , Adeno Empty 2.092 (1.032 to 3.152) 20.7 (11.2 to 30.2) A
4 Oxygen 0.1 , Adeno HIF 0.405 (0.001 to 0.808) -9.05 (-24.8 to 6.7) A
5 Oxygen 0.1 , Adeno EPAS 12.24 (7.559 to 16.921) 110.75 (64.6 to 156.9) P
Normalized Intensity
Selected : 60511_at
EGLN3
15.0
14.0
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
20 None
20 Empty
0.1 Empty
0.1 HIF
0.1 EPAS

FIG. 32h

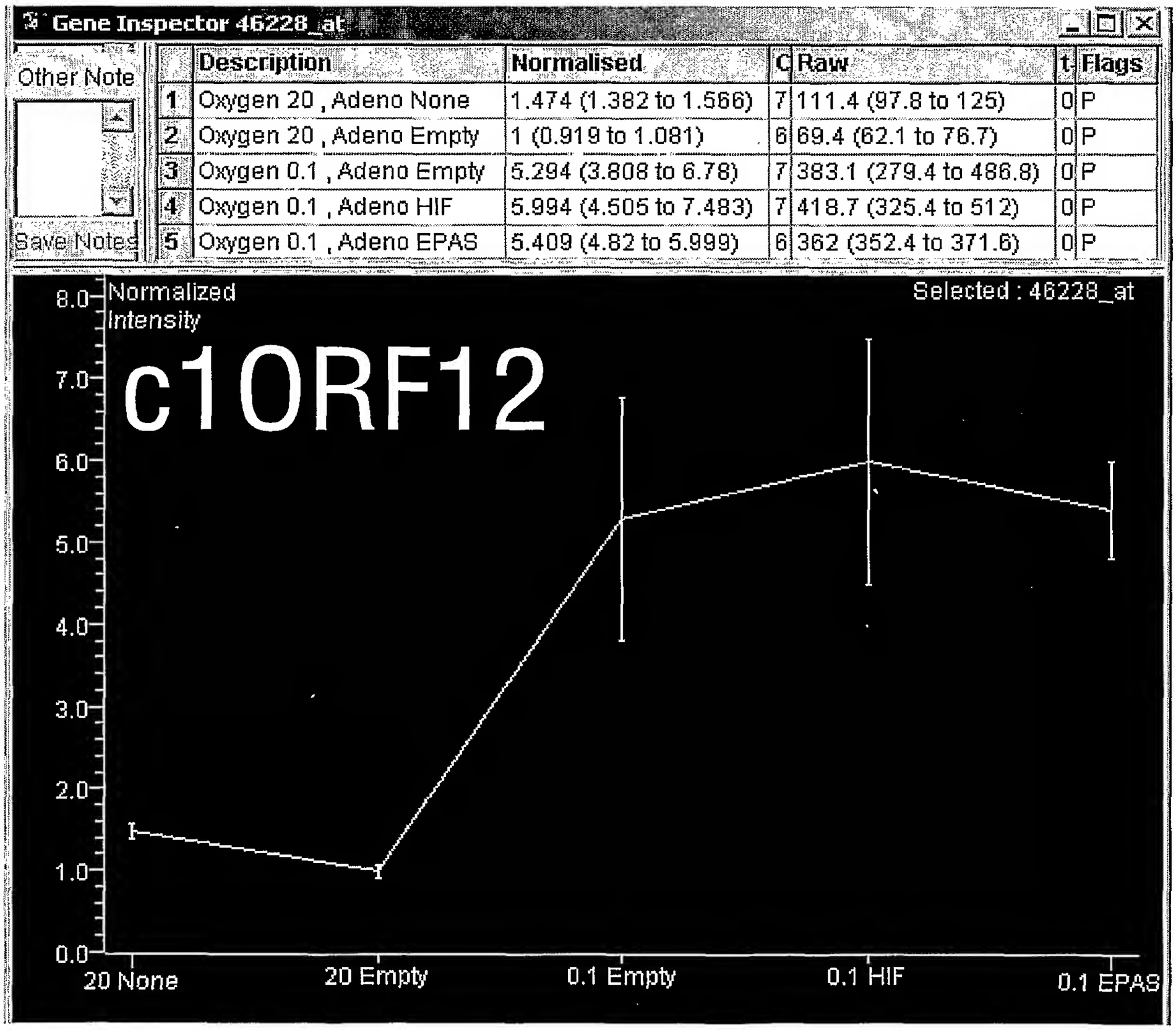

Gene Inspector 46228_at
Other Note
Save Notes
Description
Normalised
C
Raw
t
Flags
1 Oxygen 20 , Adeno None 1.474 (1.382 to 1.566) 7 111.4 (97.8 to 125) 0 P
2 Oxygen 20 , Adeno Empty 1 (0.919 to 1.081) 6 69.4 (62.1 to 76.7) 0 P
3 Oxygen 0.1 , Adeno Empty 5.294 (3.808 to 6.78) 7 383.1 (279.4 to 486.8) 0 P
4 Oxygen 0.1 , Adeno HIF 5.994 (4.505 to 7.483) 7 418.7 (325.4 to 512) 0 P
5 Oxygen 0.1 , Adeno EPAS 5.409 (4.82 to 5.999) 6 362 (352.4 to 371.6) 0 P
Normalized
Intensity
Selected : 46228_at
c10RF12
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
20 None
20 Empty
0.1 Empty
0.1 HIF
0.1 EPAS

FIG. 32i

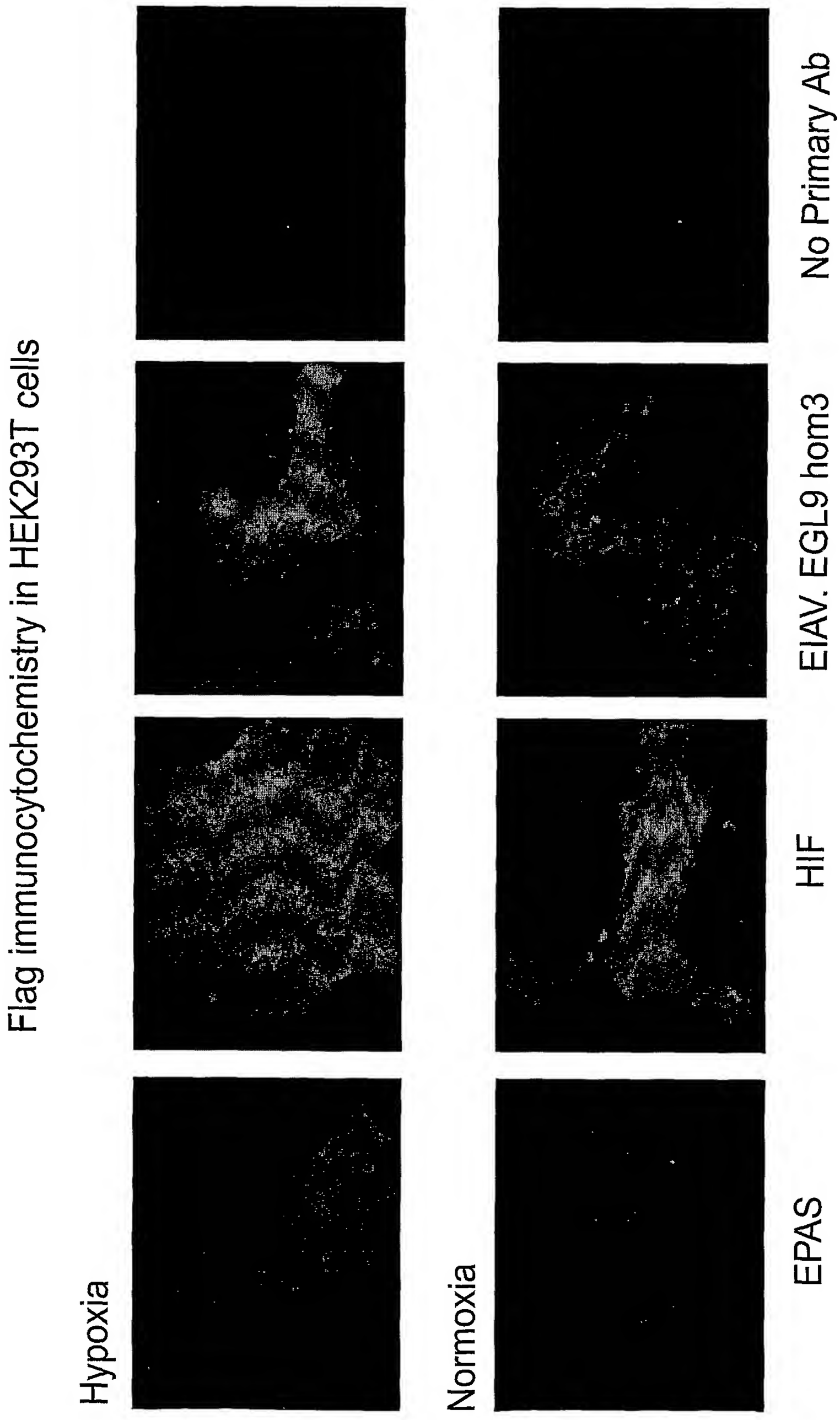

Flag immunocytochemistry in HEK293T cells
Hypoxia
Normoxia
HIF
EPAS
EIAV. EGL9 hom3
No Primary Ab

FIG. 32j

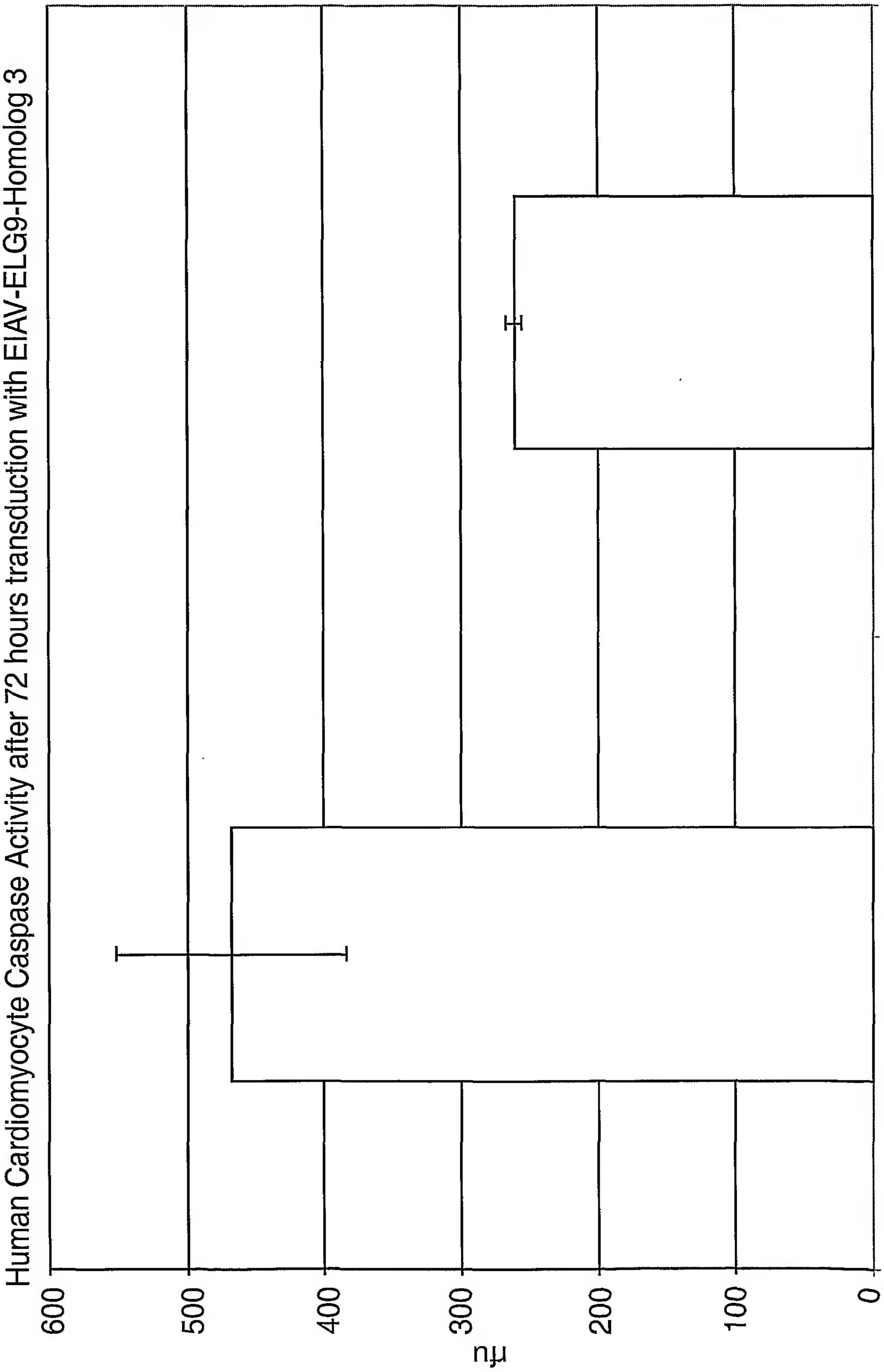

Human Cardiomyocyte Caspase Activity after 72 hours transduction with EIAV-ELG9-Homolog 3
nμ
600
500
400
300
200
100
0
EIAV-ELG9 Homolog 3
Untransduced

FIG. 33 p1E7/ SeqID:84/ Novel Metallothionein

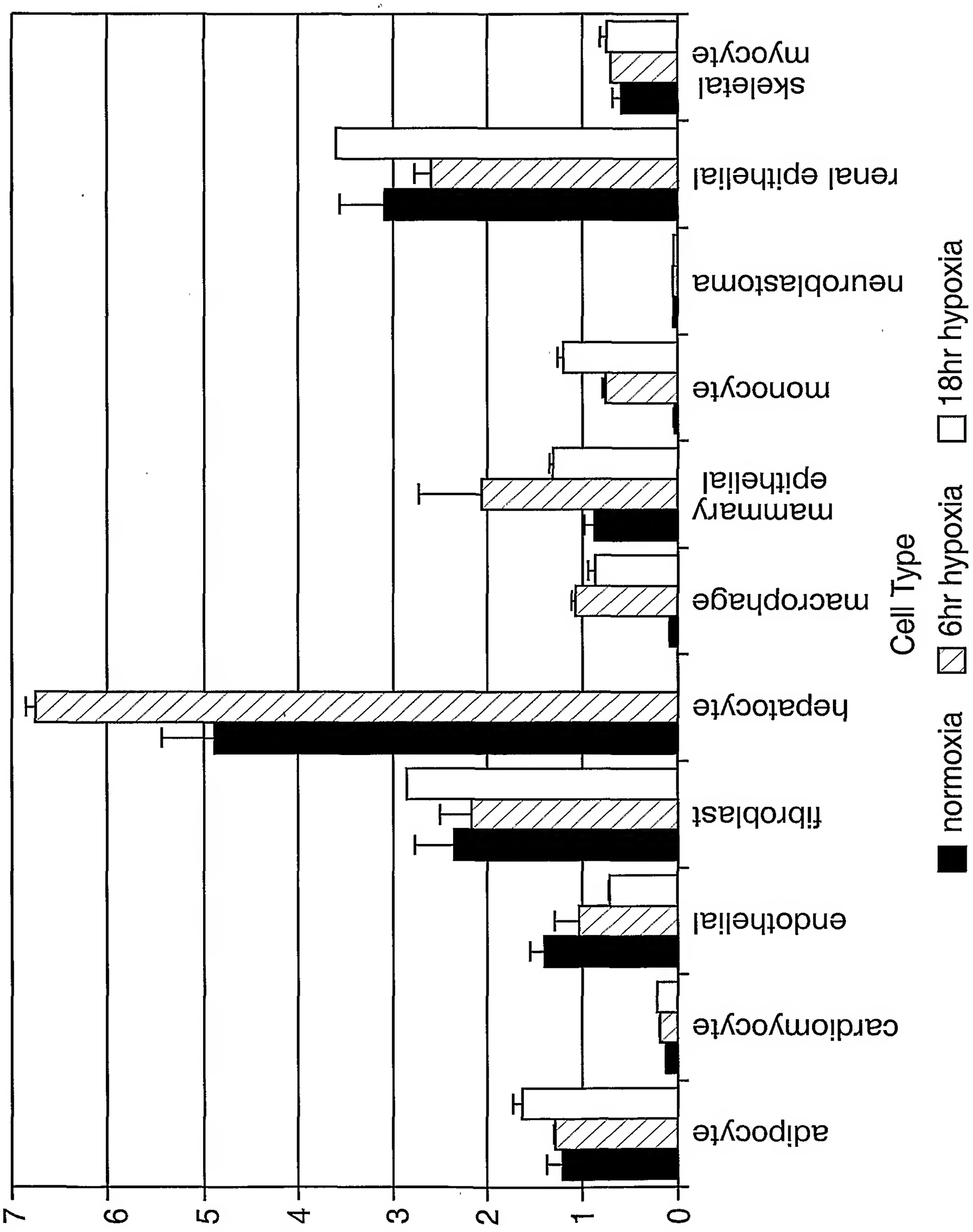


FIG. 34 p1F6/ SeqID:338/ Hypothetical protein hqp0376

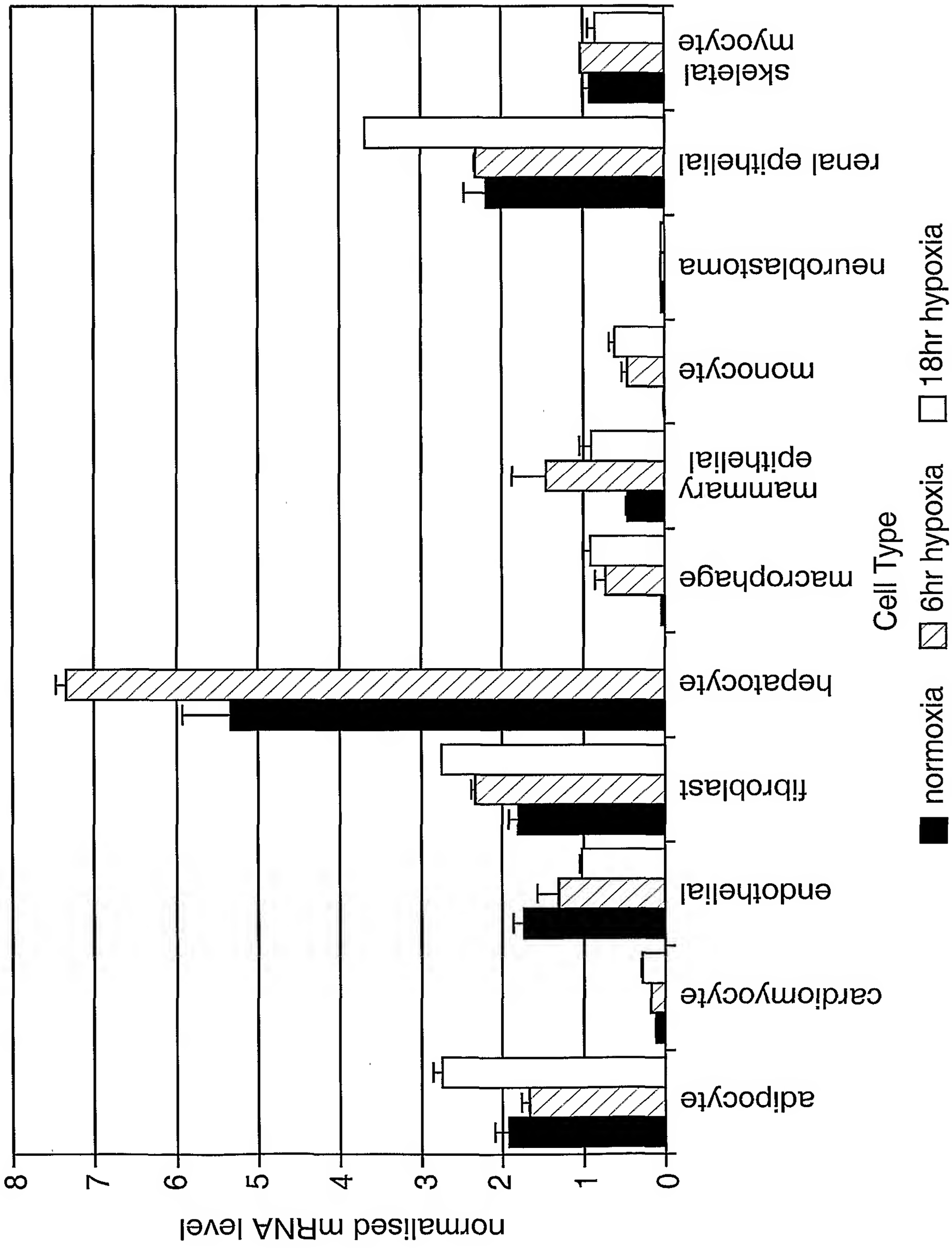


FIG. 35 p1A23/ SeqID:266/ Metallothionein 2A

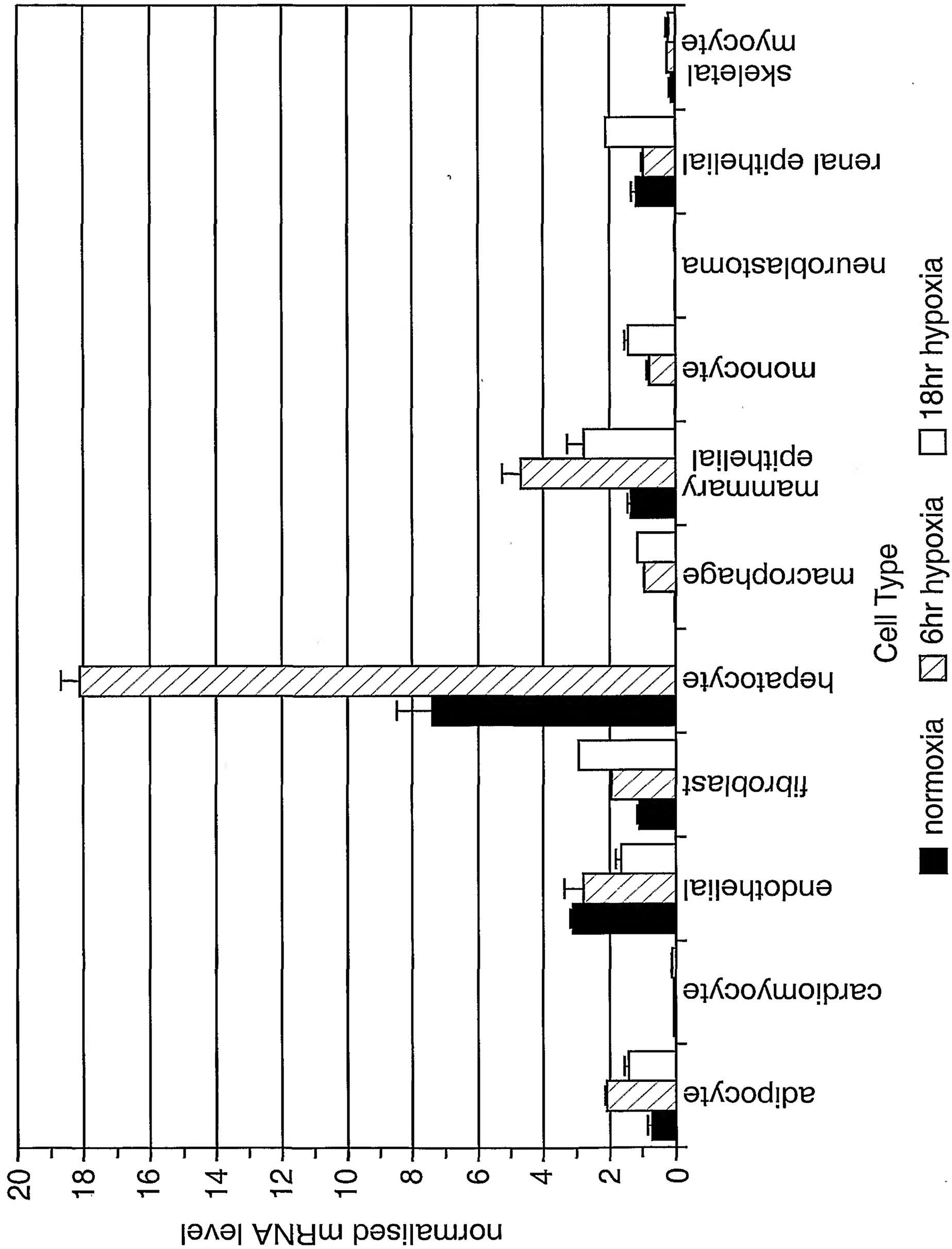


FIG. 36 p1B1/ SeqID:244/ Metallothionein 1G

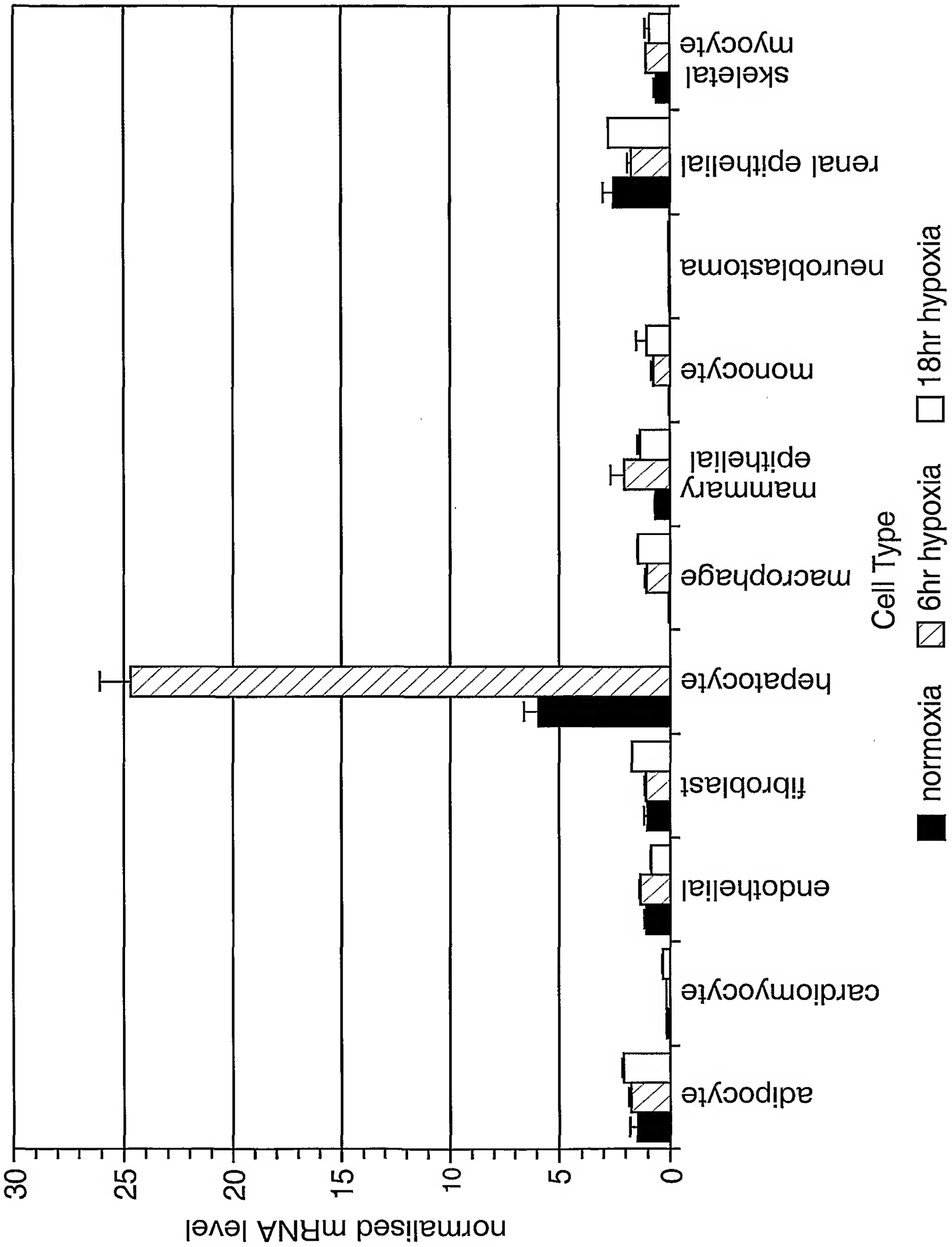


FIG. 37 p1A24/ SeqID:240/ Metallothionein 1H

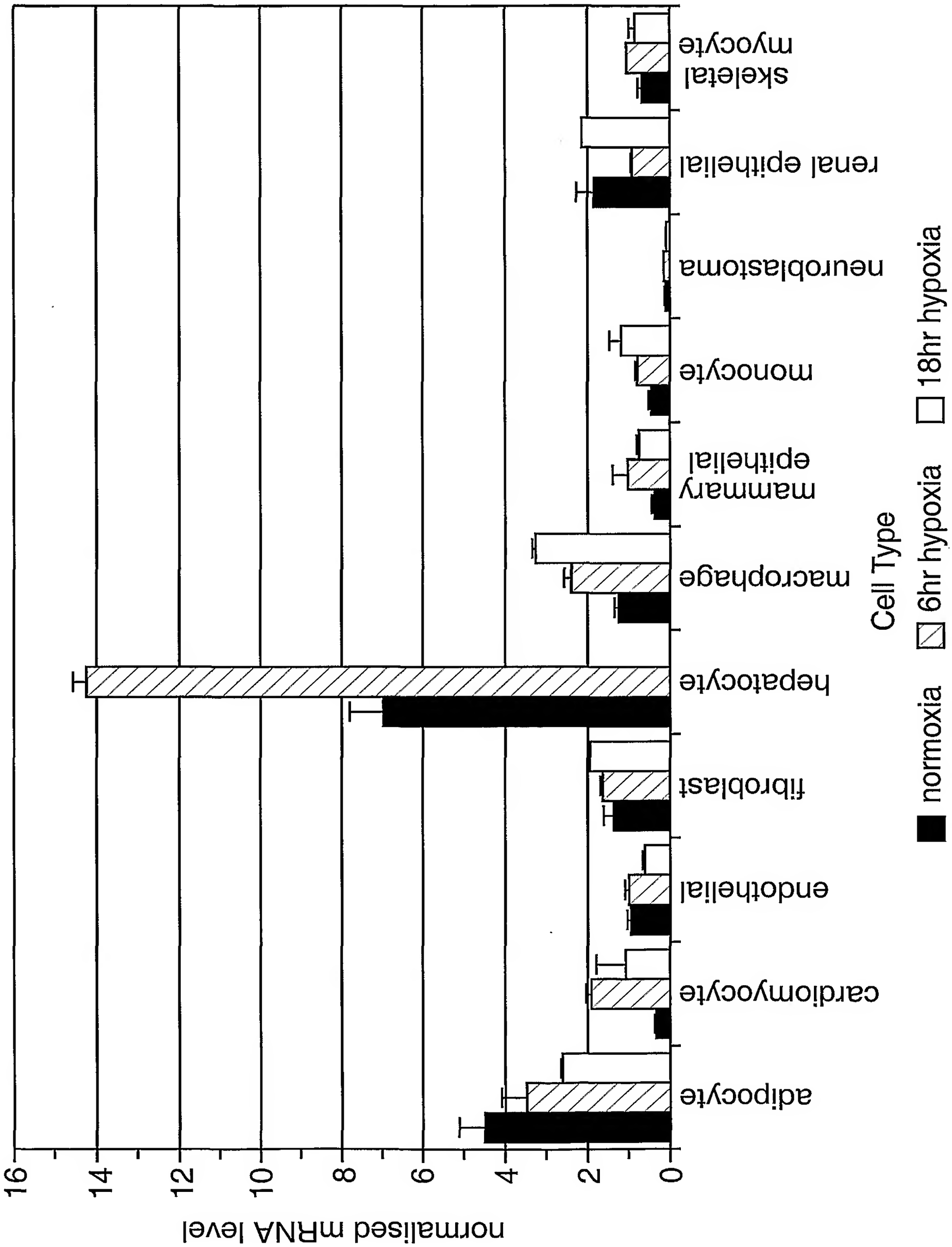


FIG. 38 p1E5/ SeqID:142/ Hepcidin antimicrobial peptide

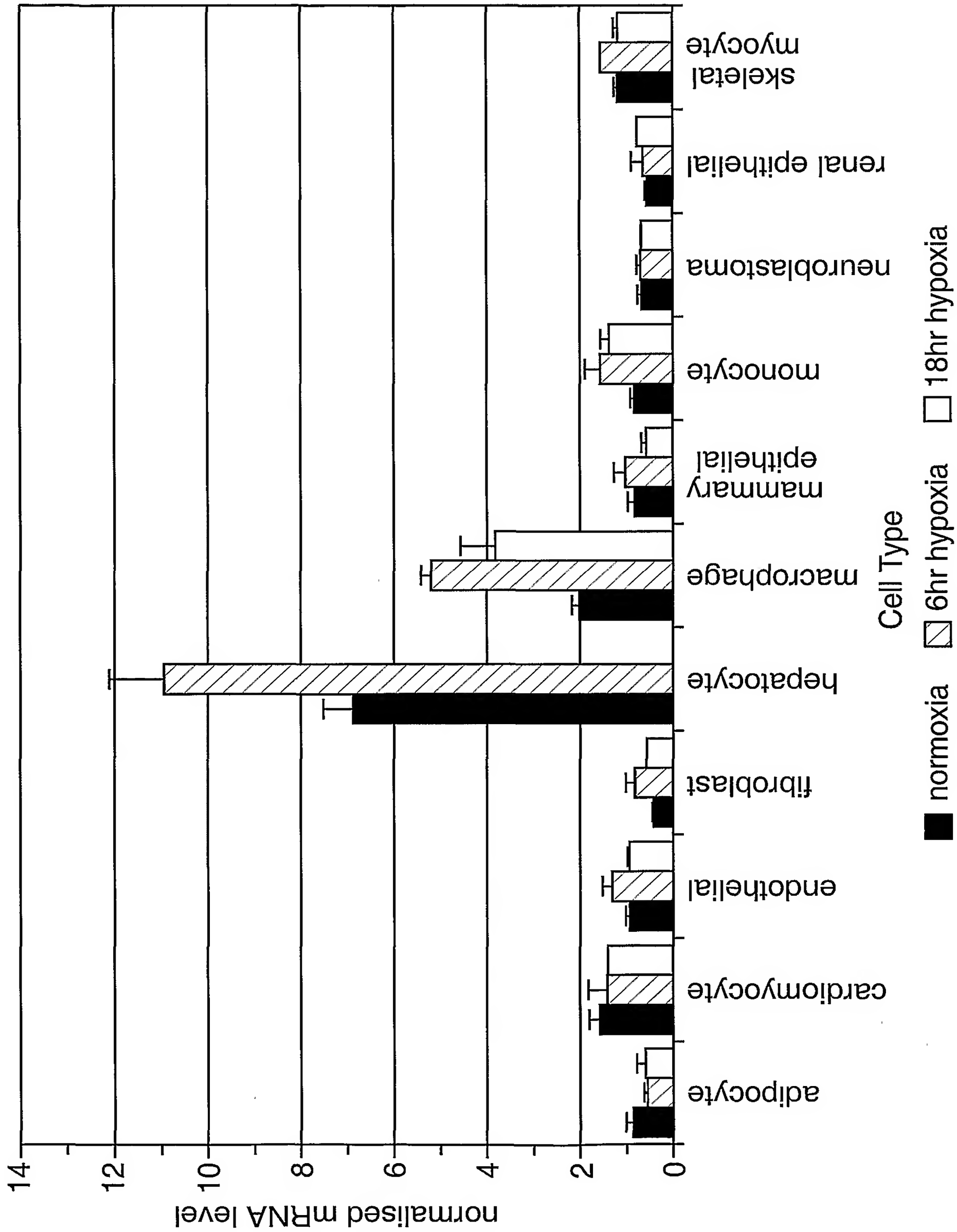
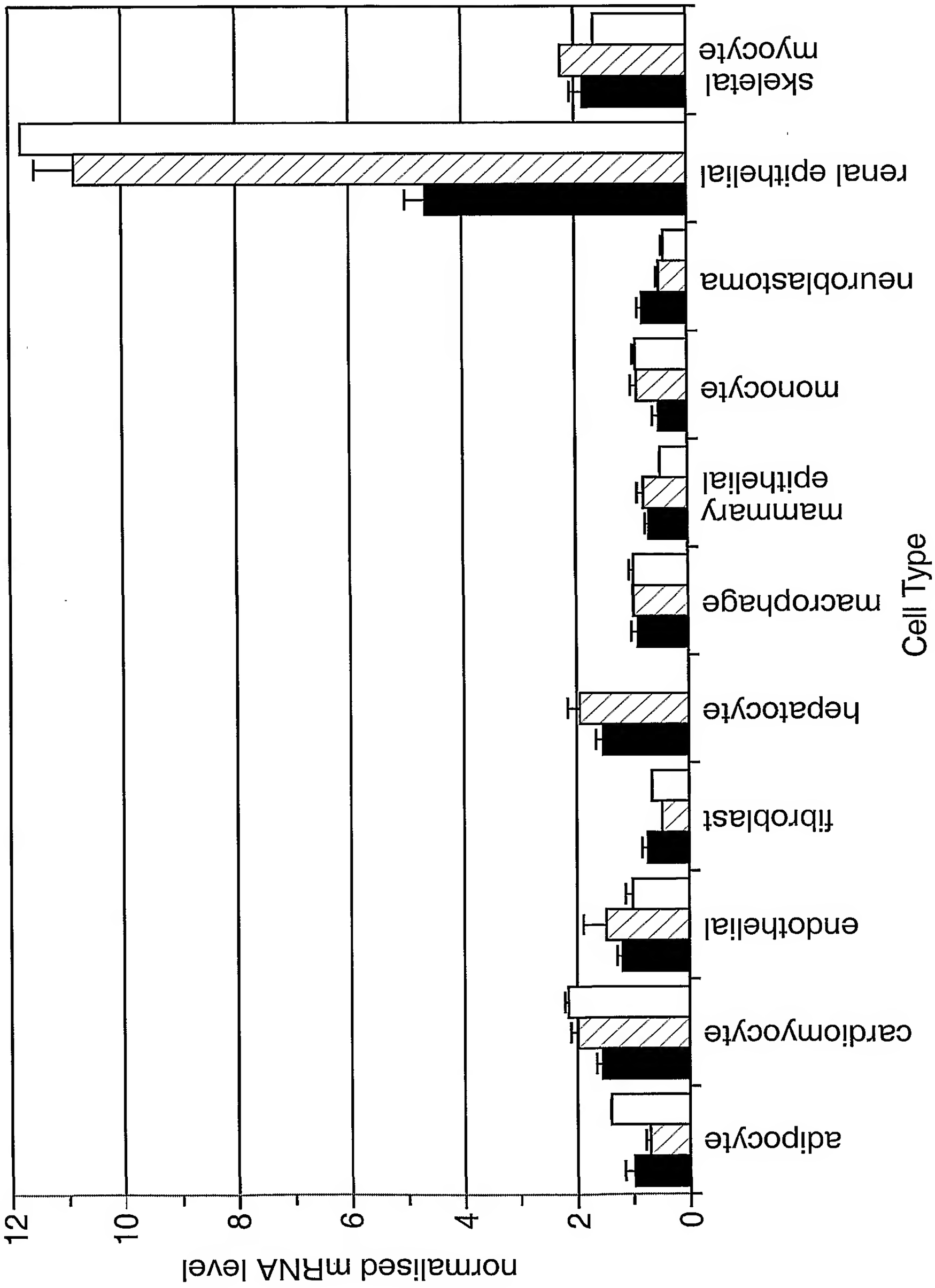


FIG. 39 p1D24/ SeqID:118/ EST



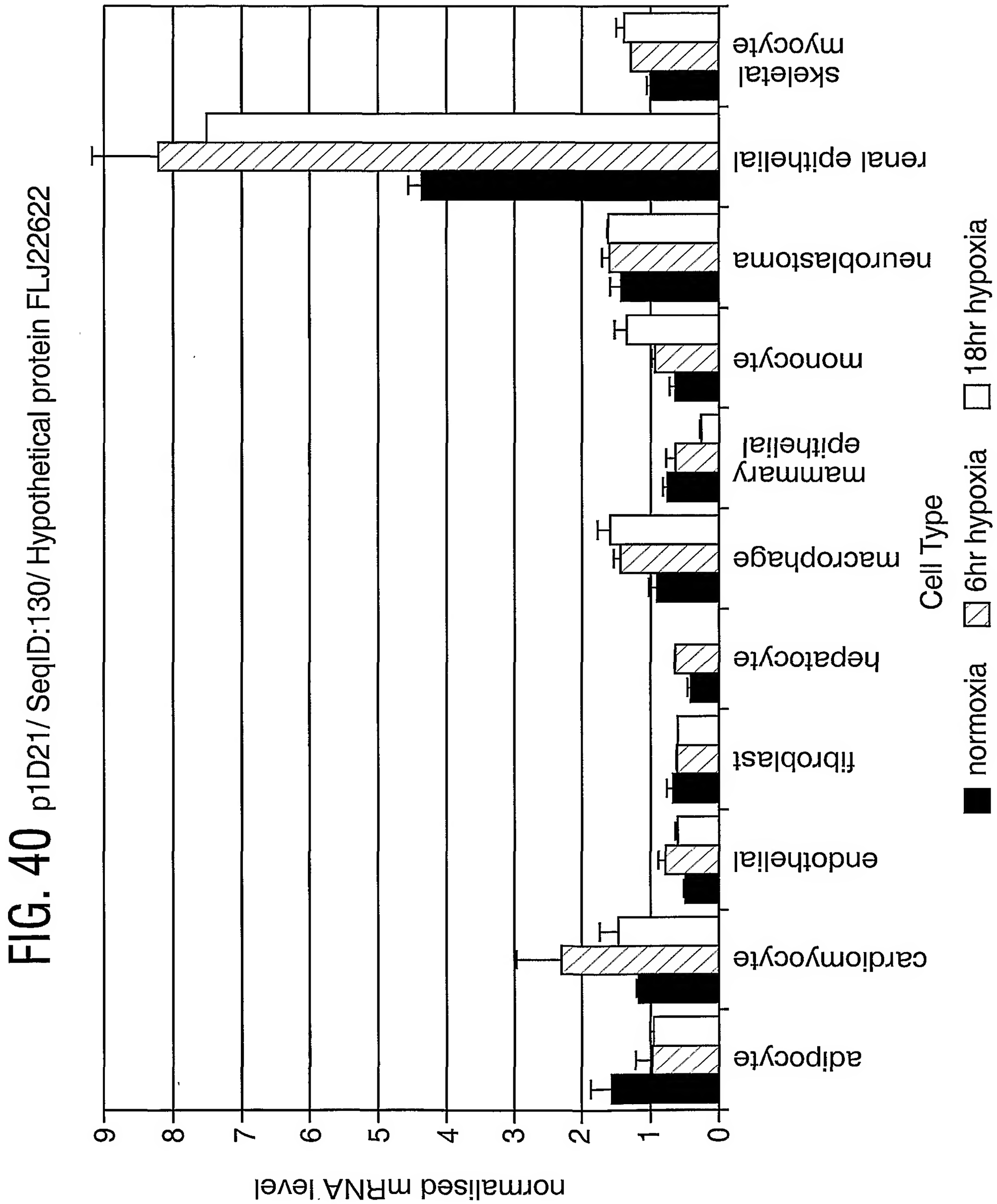


FIG. 40 p1D21/ SeqID:130/ Hypothetical protein FLJ22622

FIG. 41 p1D15/ SeqID:32/ TRIP-Br2

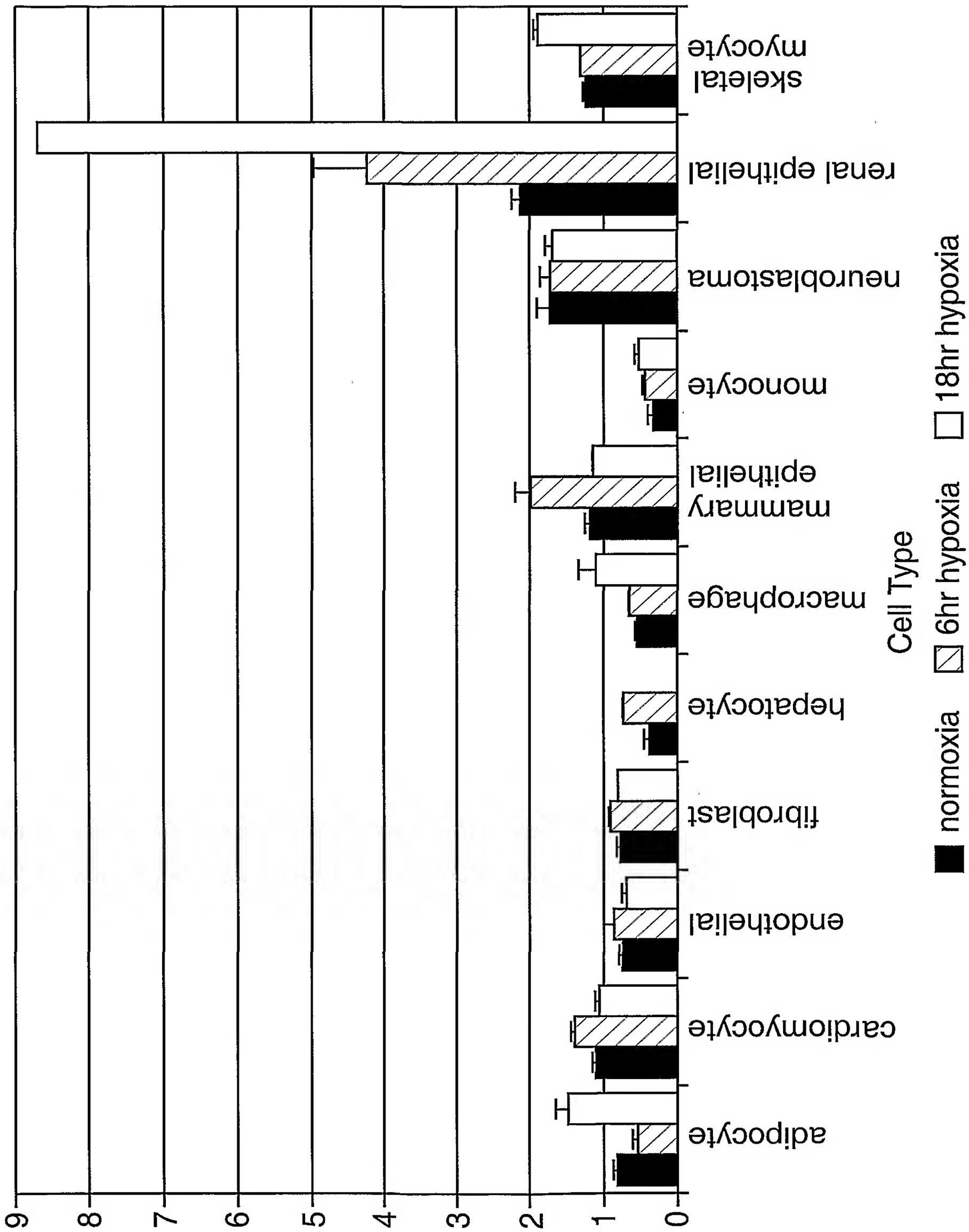


FIG. 42 p1G11/ SeqID:302/ Tumor protein D52

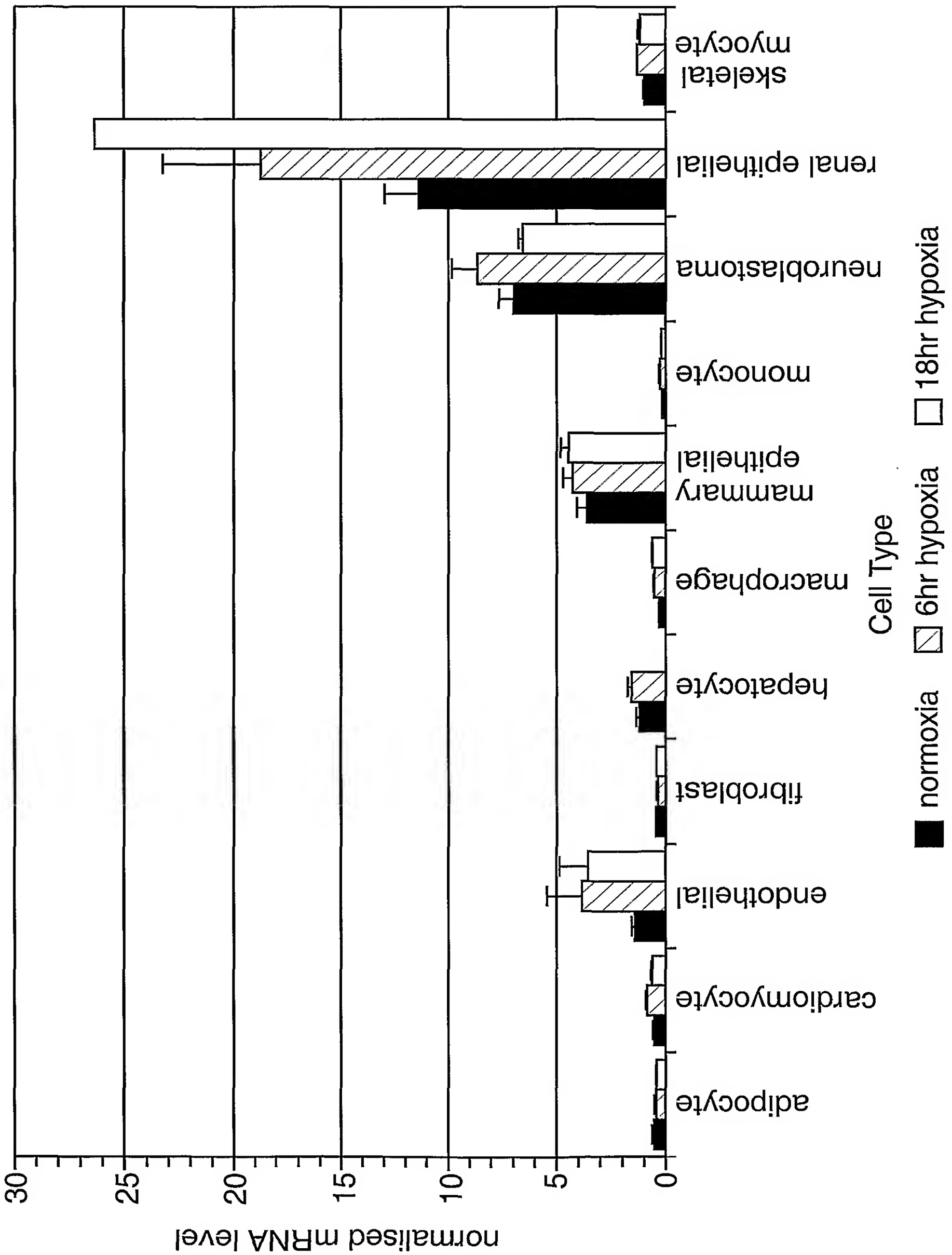


FIG. 43 p1P14/ SeqID:92/ Semaphorin 4b

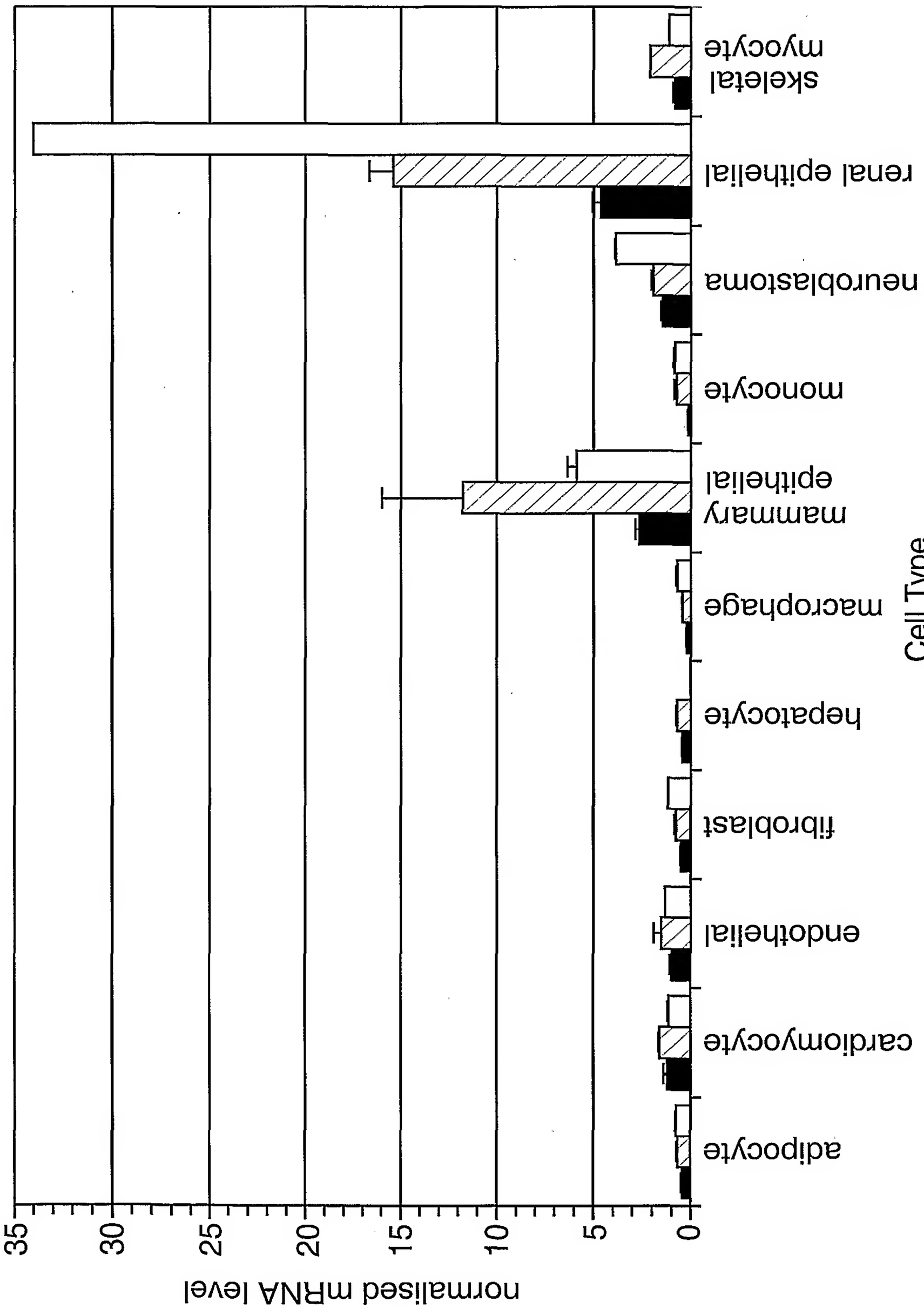


FIG. 44 p1C8/ SeqID:372/ Dec-1

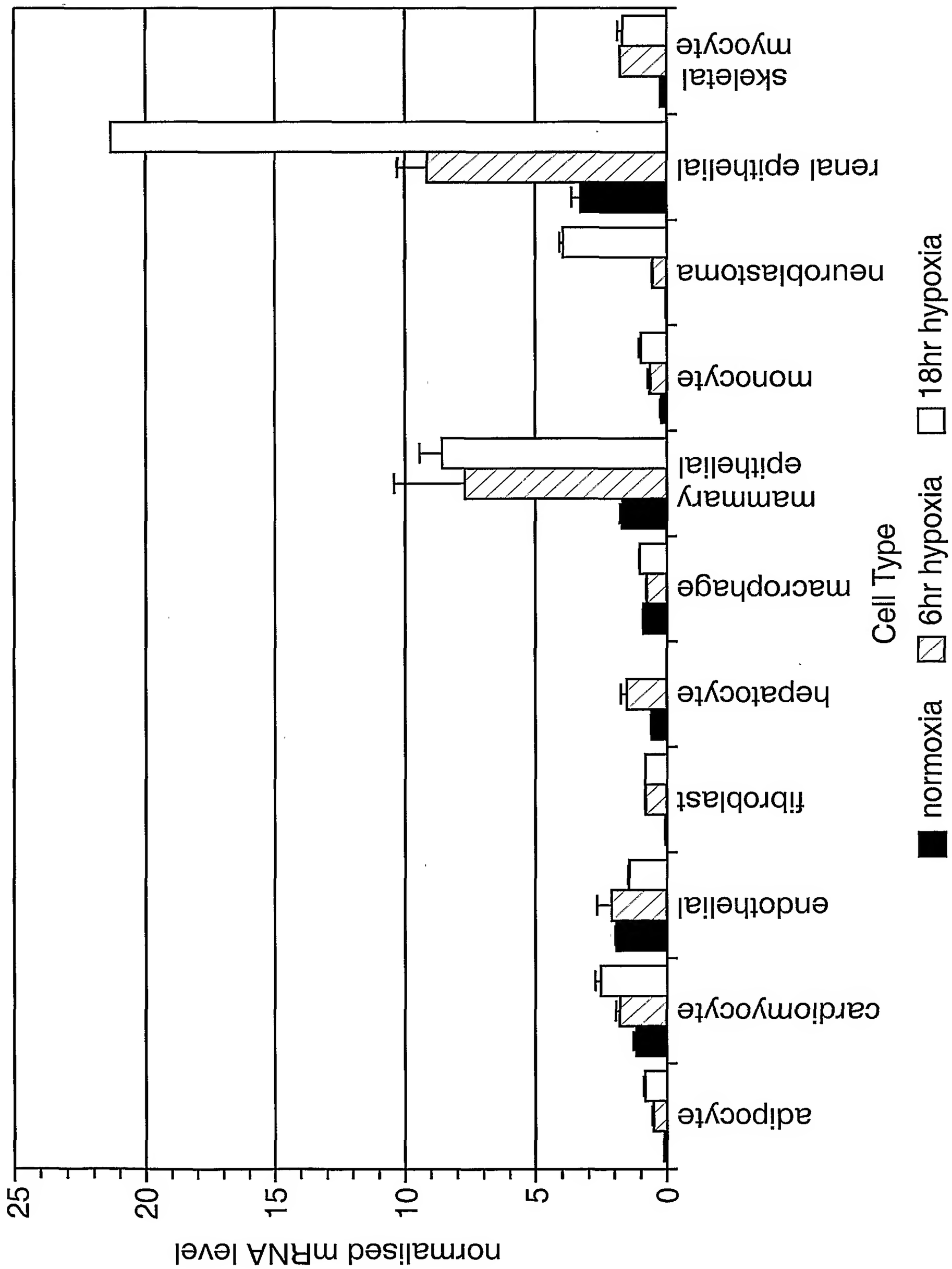


FIG. 45 p1J23/ SeqID:448/ Calgranulin A

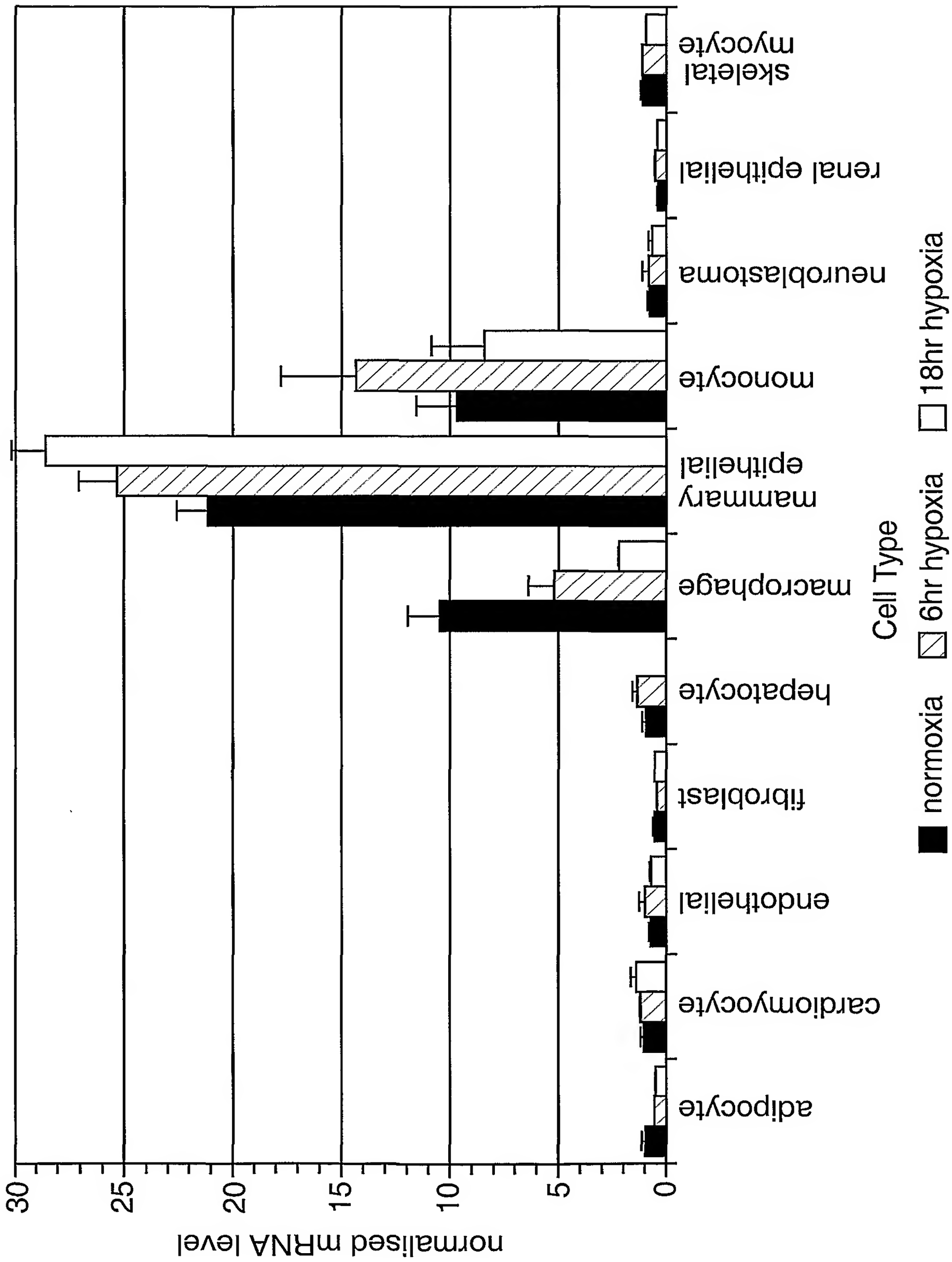
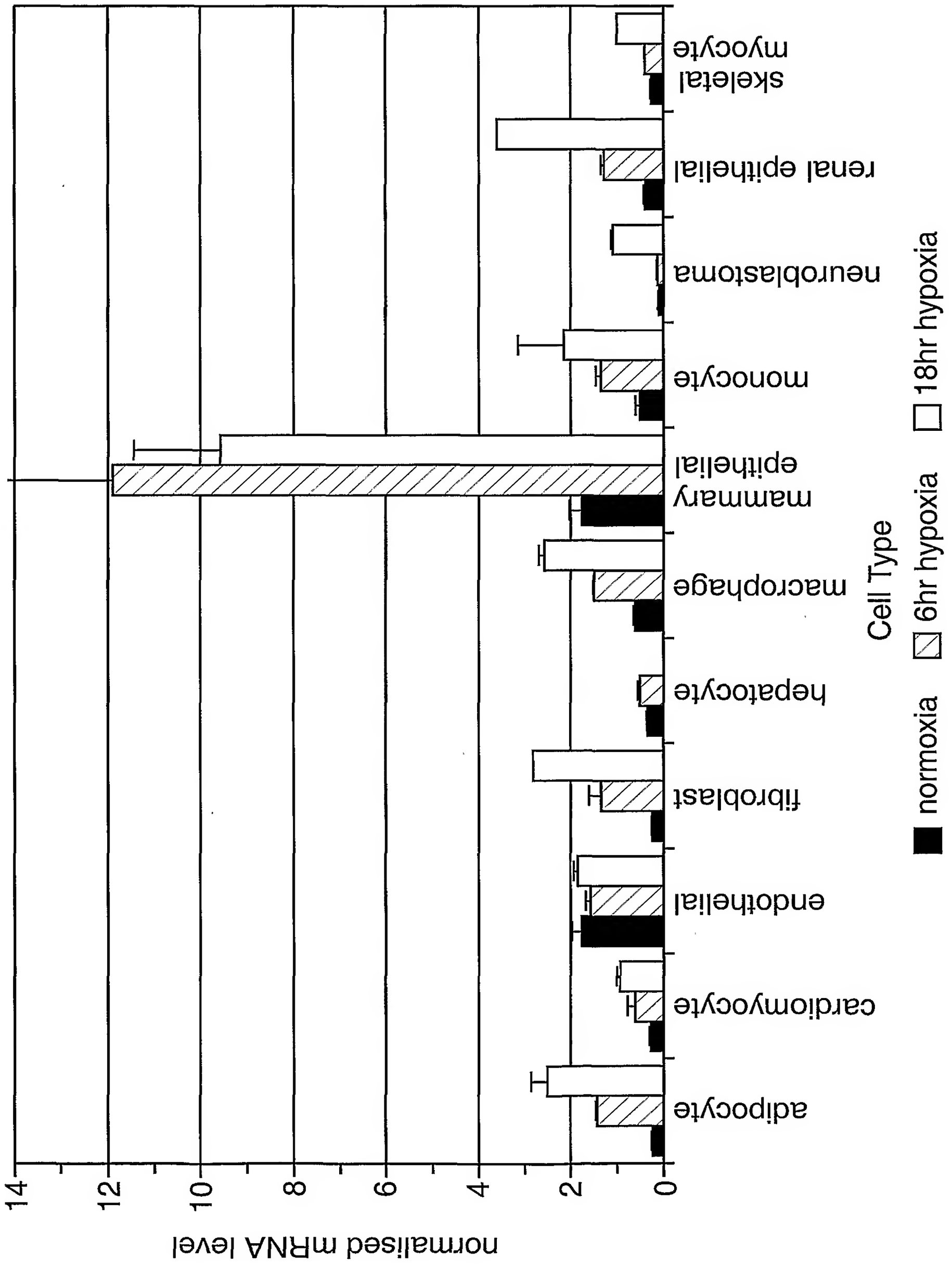


FIG. 46 p1D6/ SeqID:68/ ERO1 (S. cerevisiae)-like



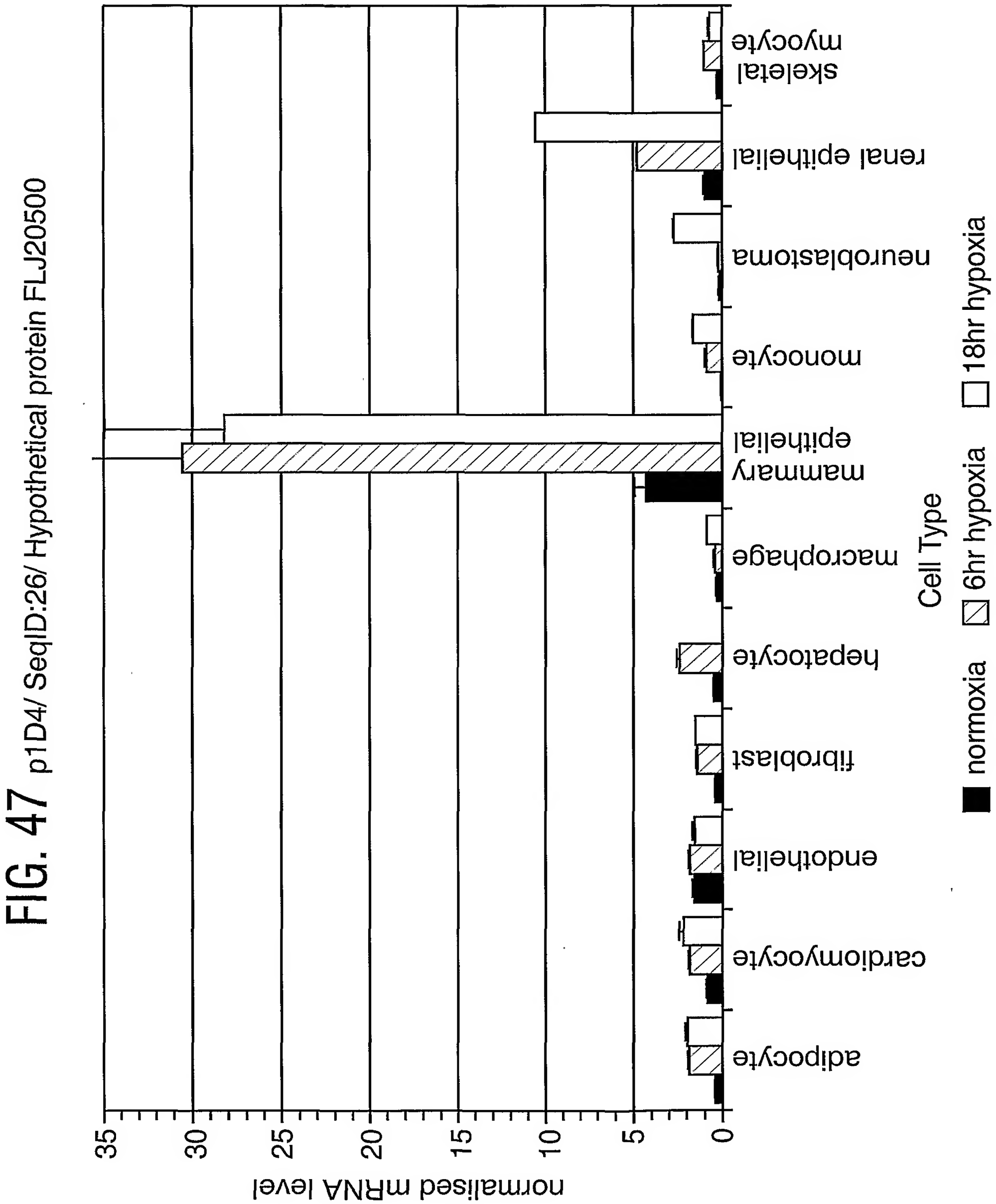
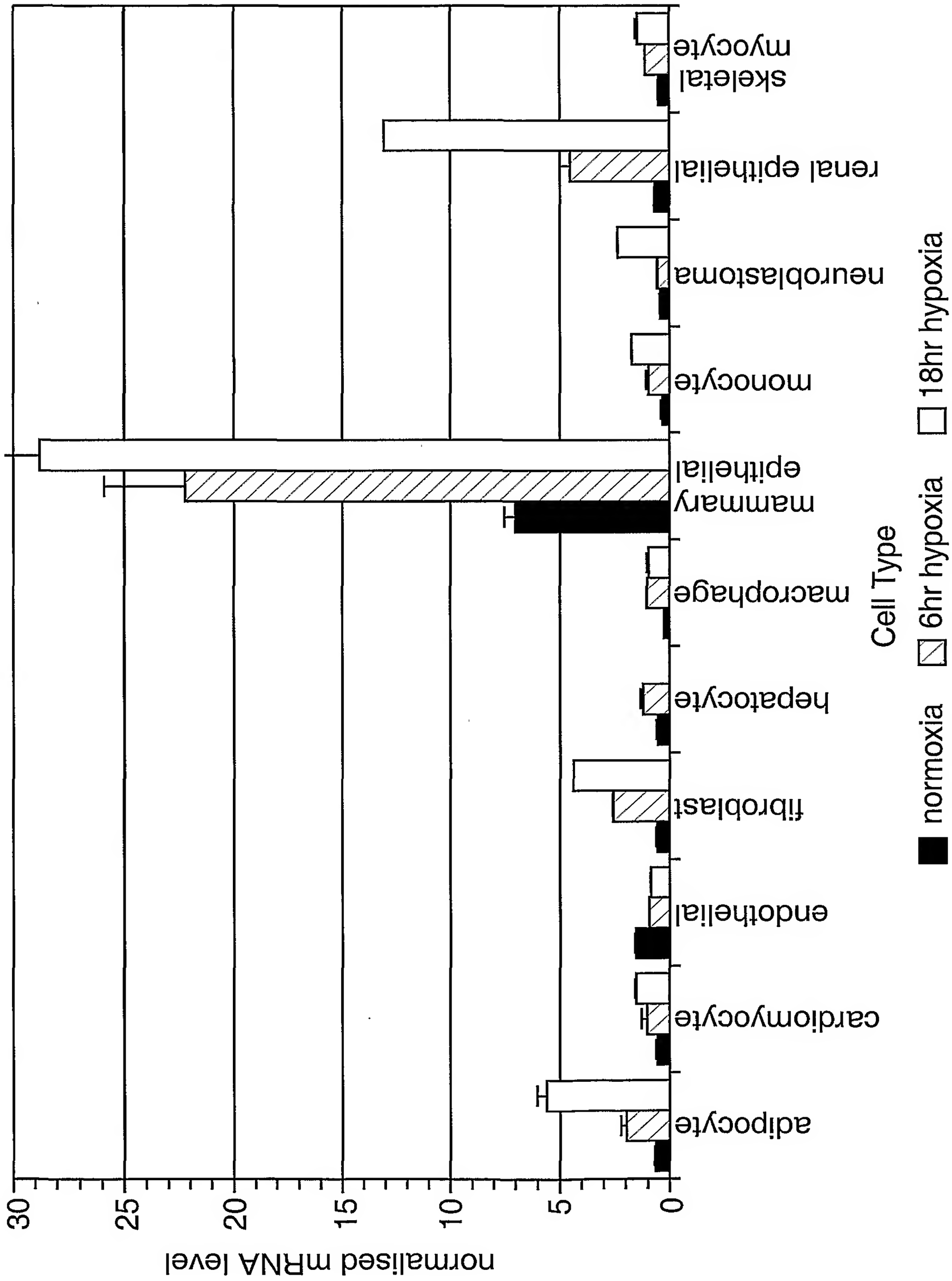


FIG. 47 p1D4/ SeqID:26/ Hypothetical protein FLJ20500
normalised mRNA level
0
5
10
15
20
25
30
35
adipocyte
cardiomyocyte
endothelial
fibroblast
hepatocyte
macrophage
mammary epithelial
monocyte
neuroblastoma
renal epithelial
skeletal myocyte
Cell Type
normoxia
6hr hypoxia
18hr hypoxia

FIG. 48 p1B2/ SeqID:230/ N-myc downstream regulated



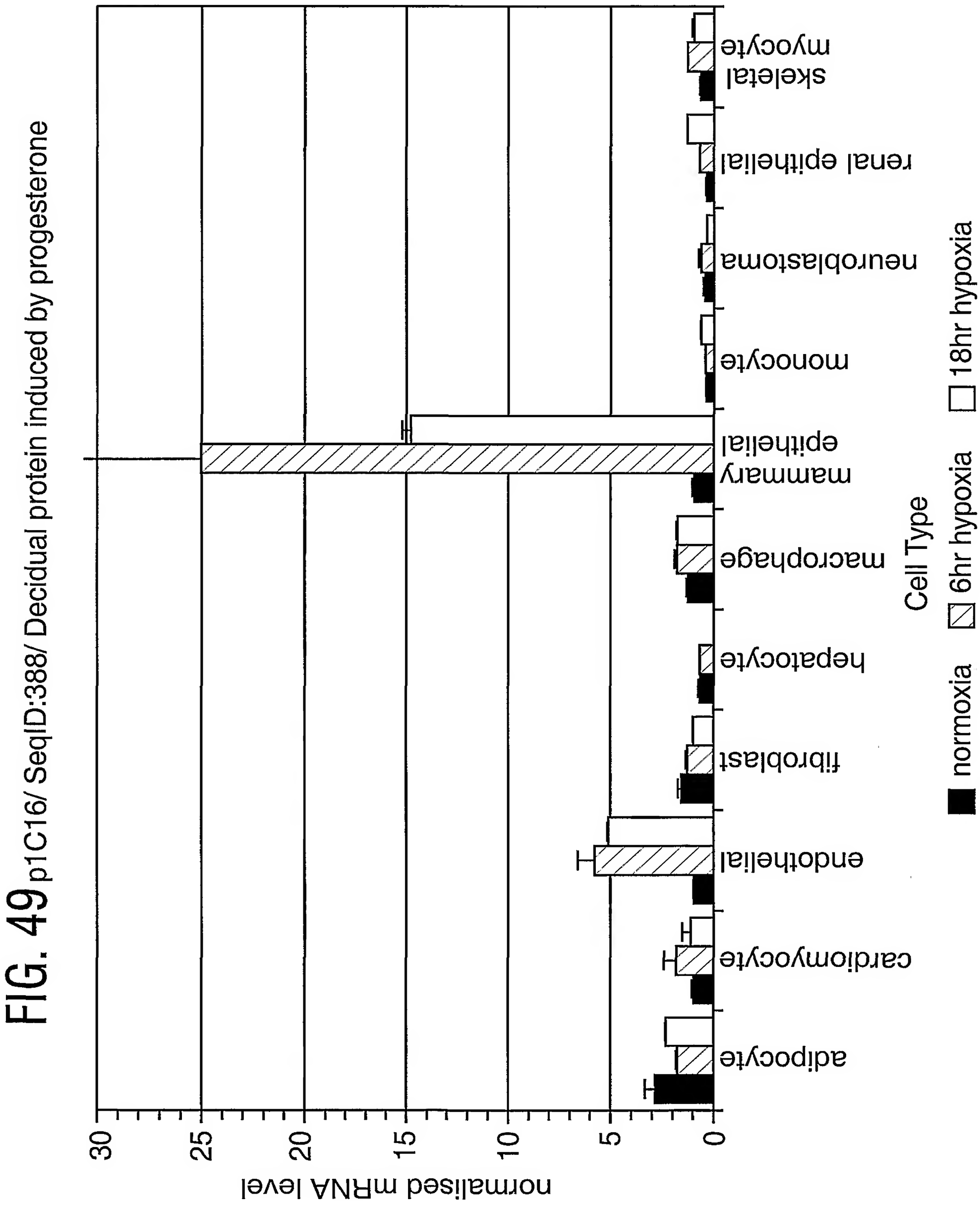


FIG. 49 p1C16/ SeqID:388/ Decidual protein induced by progesterone

FIG. 50 p1C12/ SeqID:380/ Integrin, alpha 5

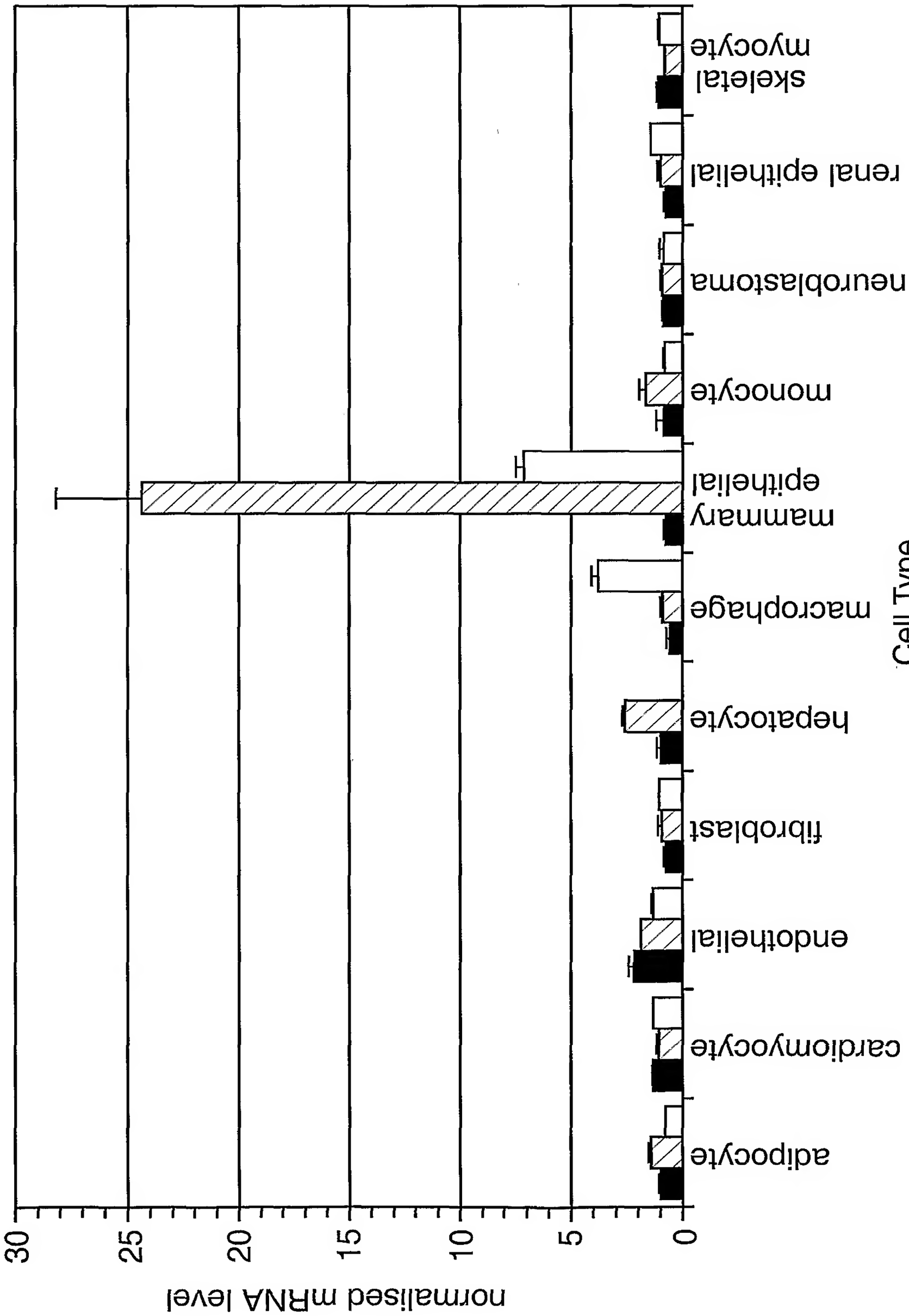


FIG. 51 p1B17/ SeqID:226/ Tissue factor

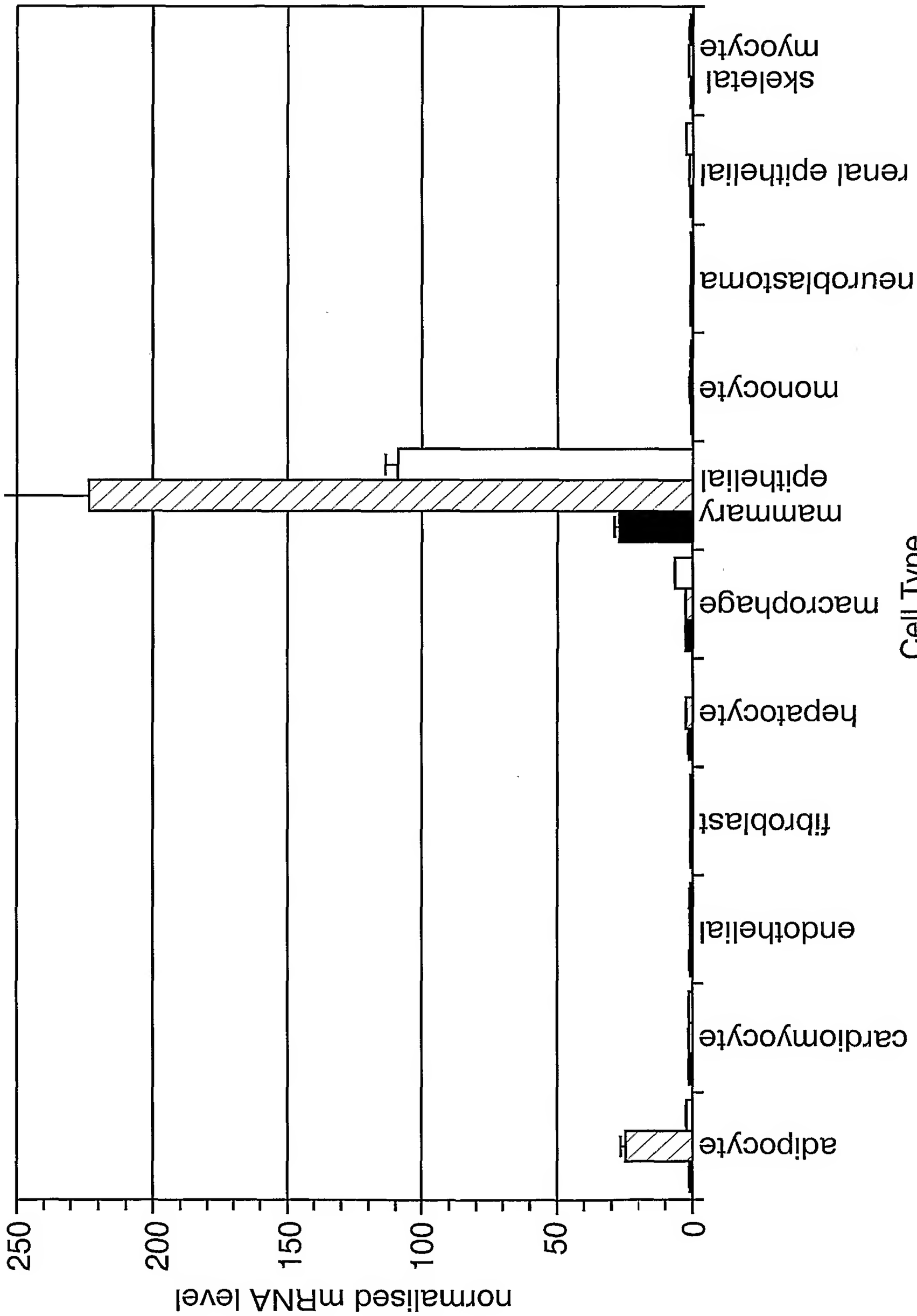


FIG. 52 p1N17/ SeqID:238/ COX-2

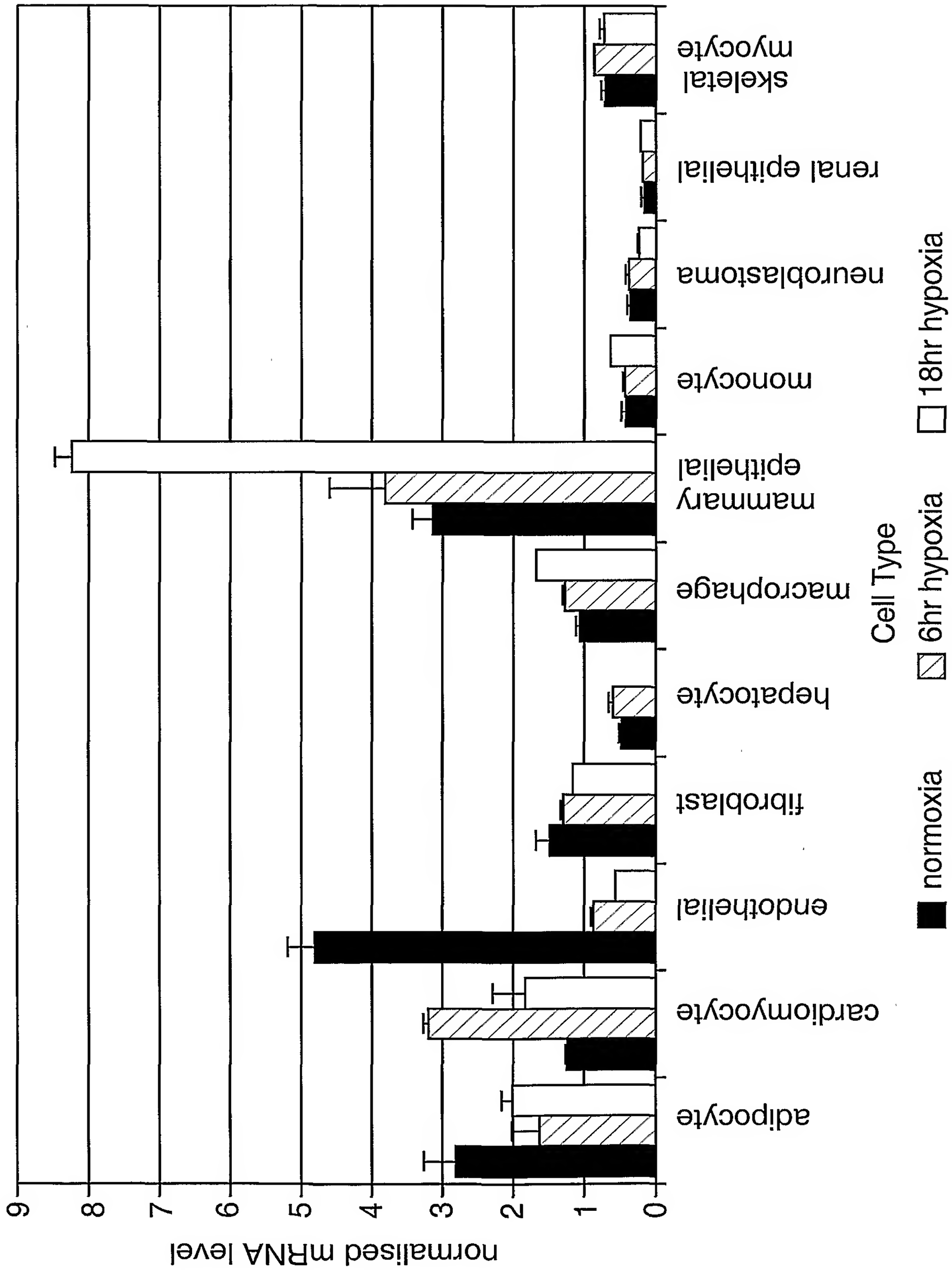


FIG. 53a

p1E10/ SeqID:72
cDNA FLJ11041 fis, clone PLACE1004405

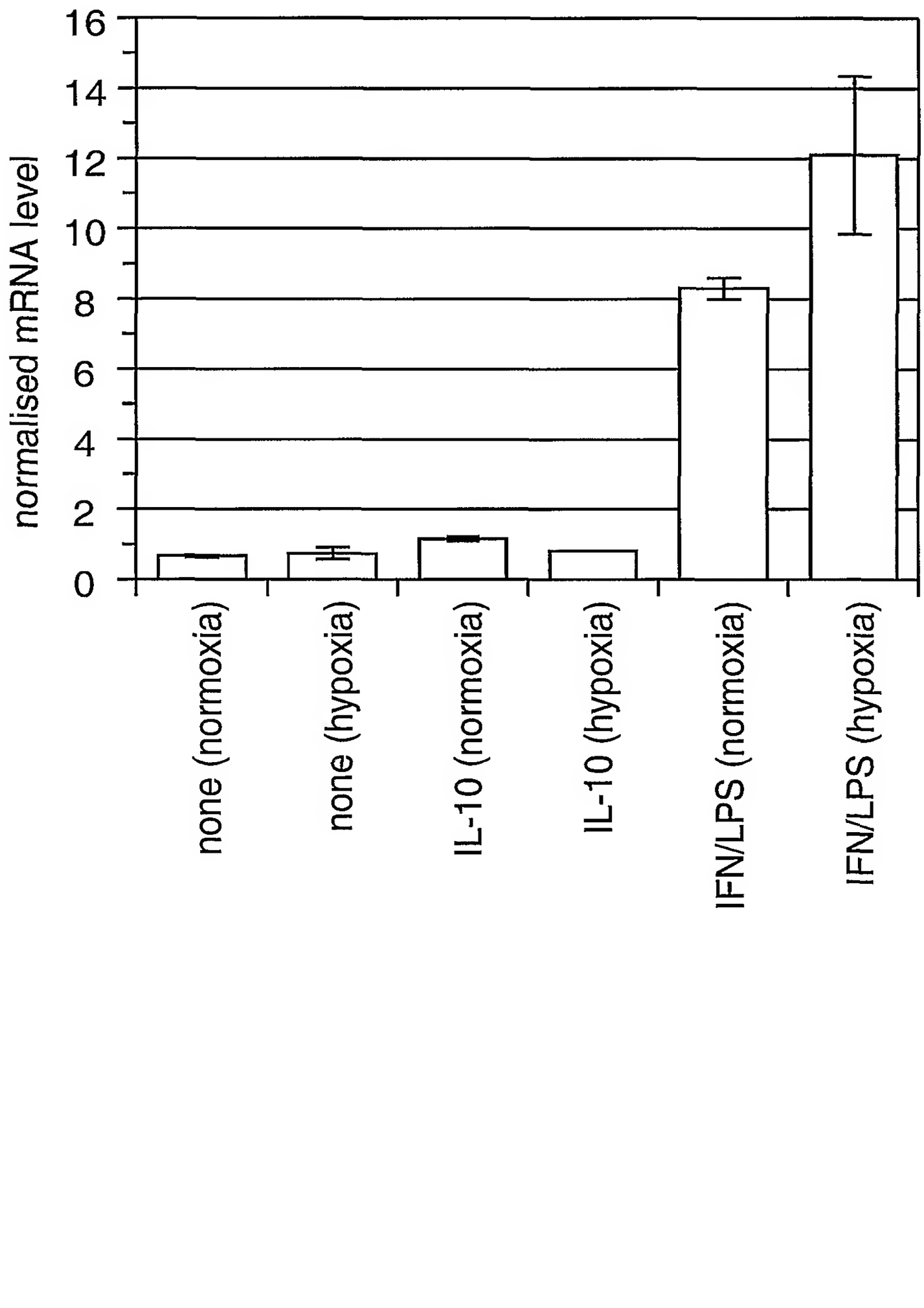


FIG. 53b

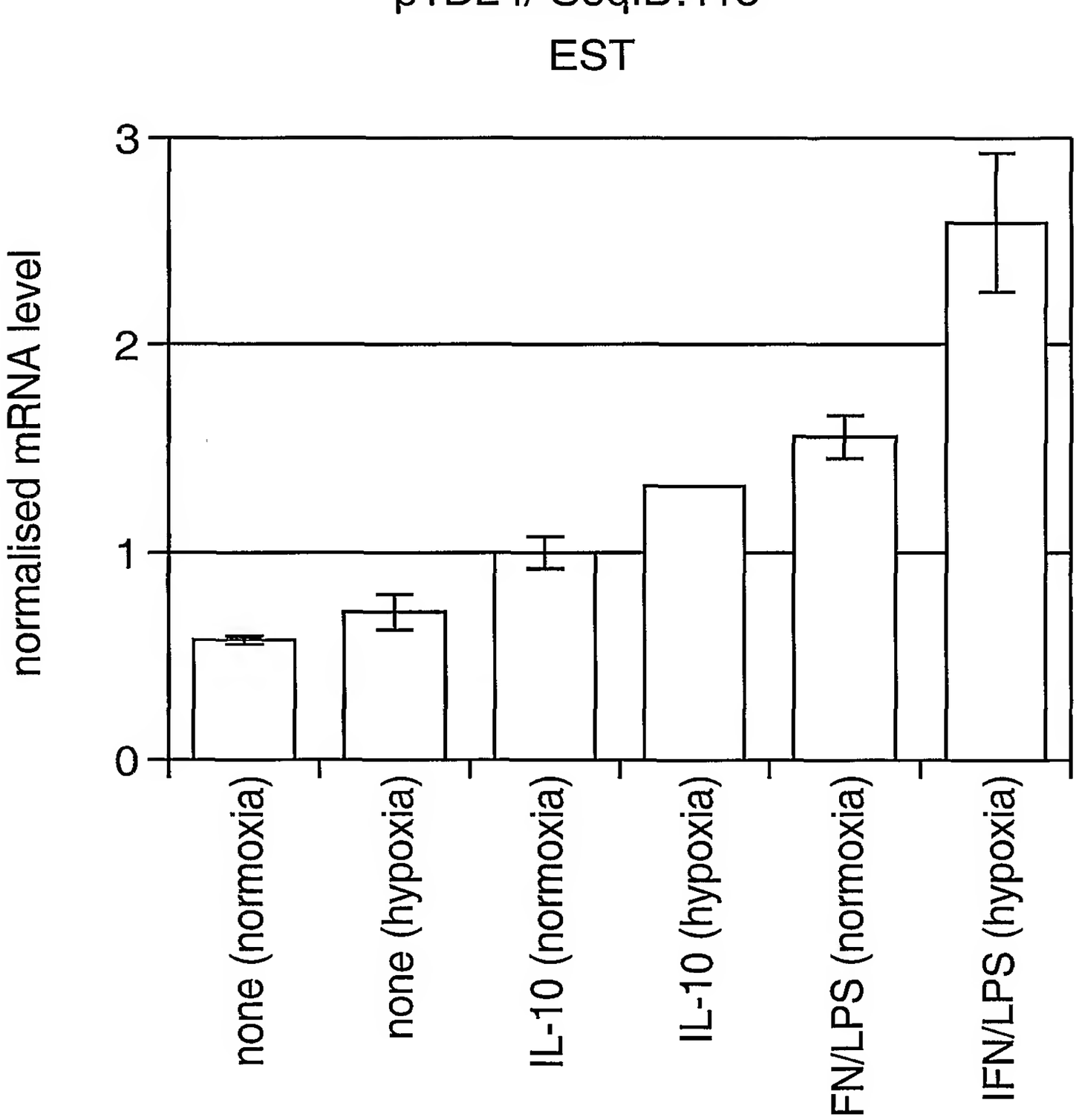

p1D24/ SeqID:118
EST
normalised mRNA level
0
1
2
3
none (normoxia)
none (hypoxia)
IL-10 (normoxia)
IL-10 (hypoxia)
IFN/LPS (normoxia)
IFN/LPS (hypoxia)

FIG. 53c

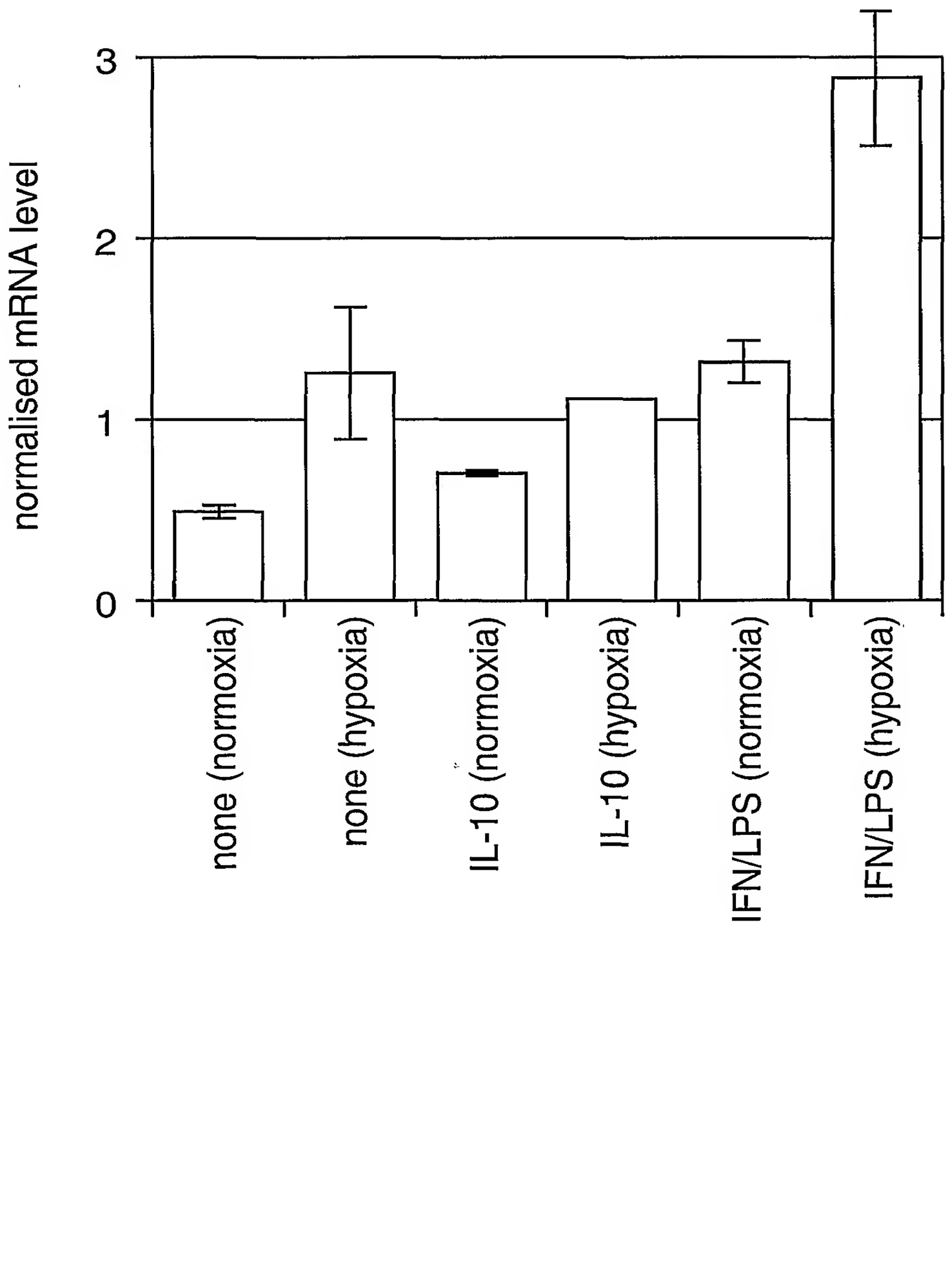

p1E7/ SeqID:84
Novel metallothionein
normalised mRNA level
0
1
2
3
none (normoxi a)
none (hypoxi a)
IL-10 (normoxi a)
IL-10 (hypoxi a)
IFN/LPS (normoxi a)
IFN/LPS (hypoxi a)

FIG. 53d

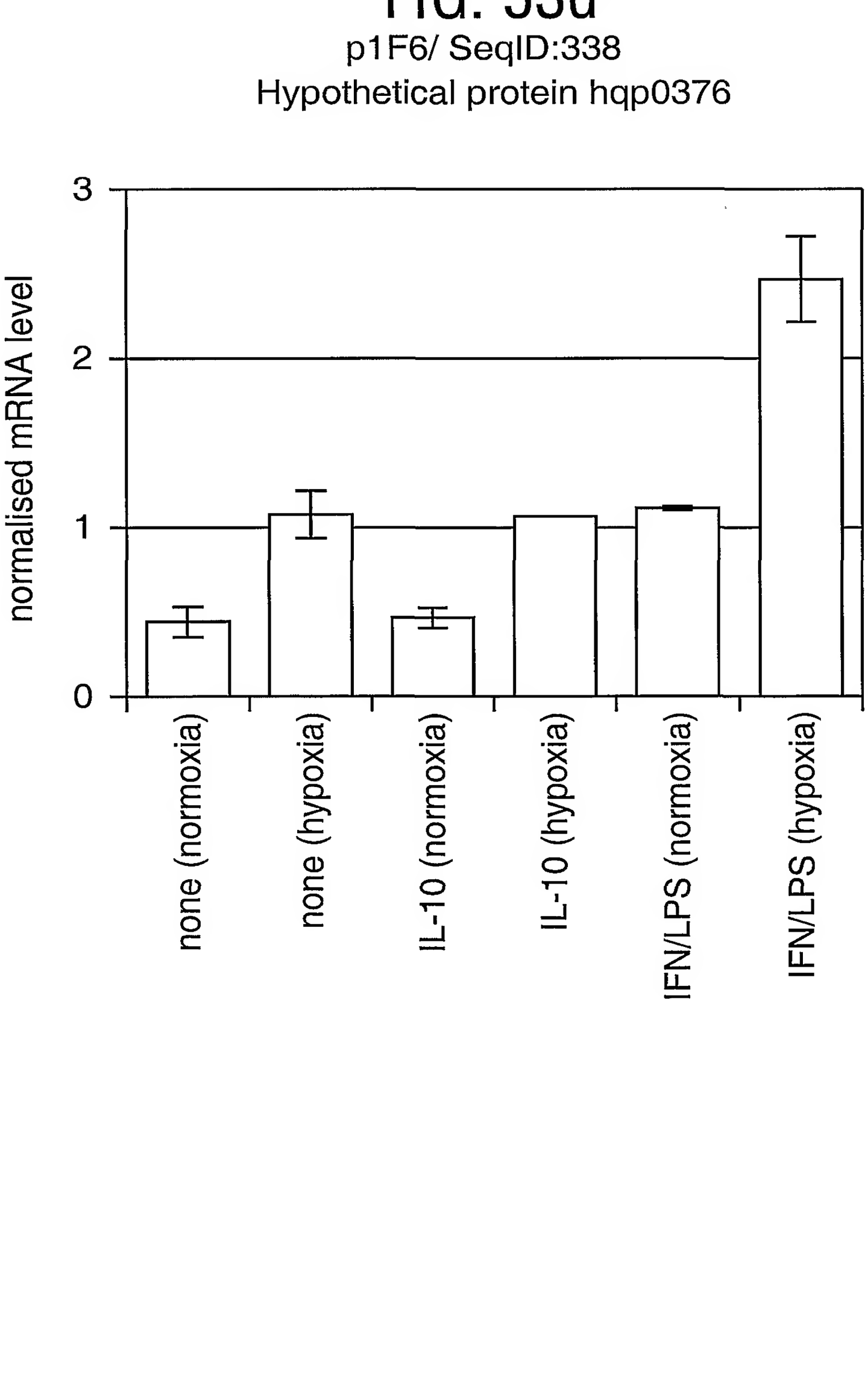

p1F6/ SeqID:338
Hypothetical protein hqp0376
normalised mRNA level
0
1
2
3
none (normoxia)
none (hypoxia)
IL-10 (normoxia)
IL-10 (hypoxia)
IFN/LPS (normoxia)
IFN/LPS (hypoxia)

FIG. 53e

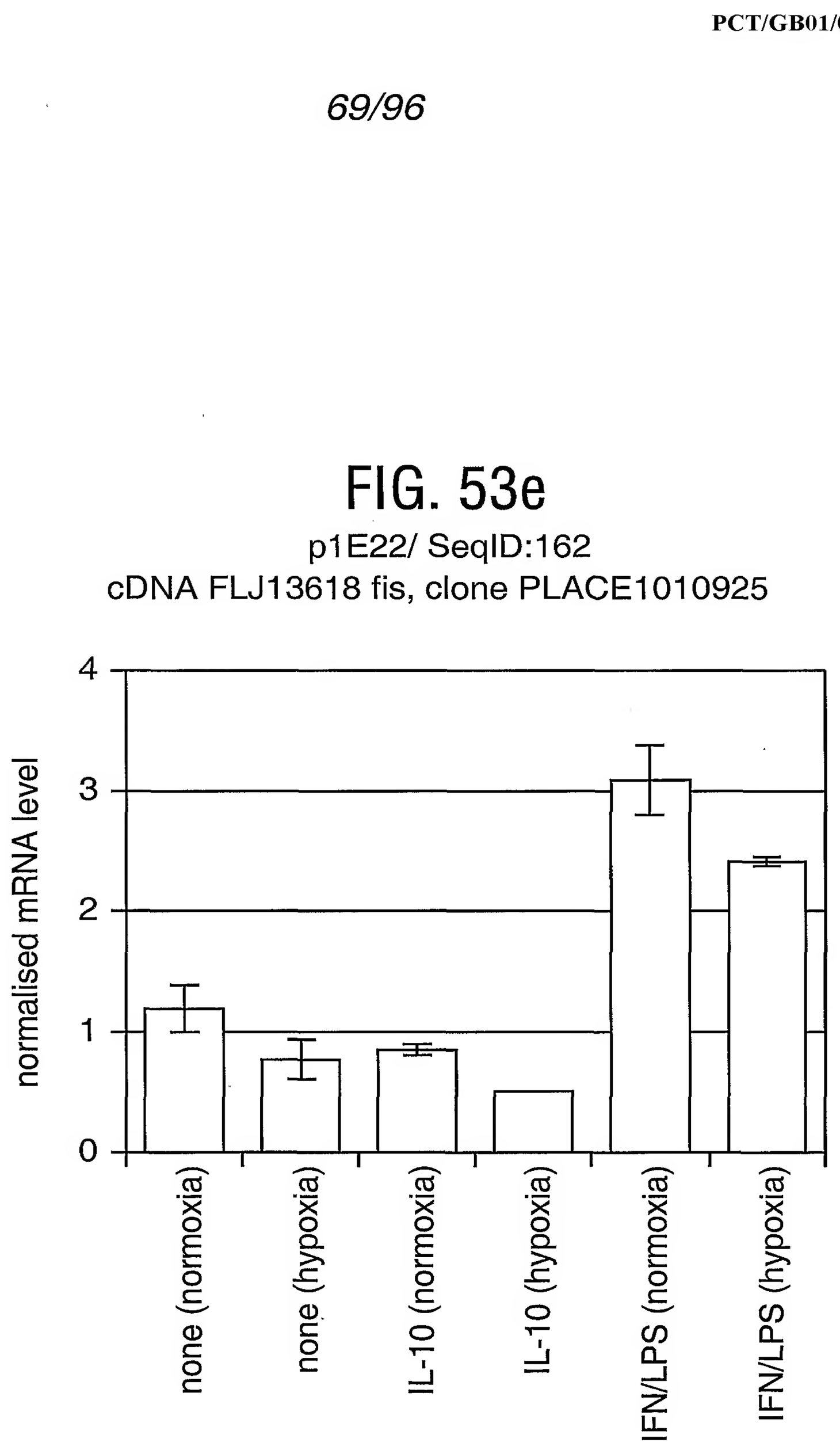

p1E22/ SeqID:162
cDNA FLJ13618 fis, clone PLACE1010925
normalised mRNA level
0
1
2
3
4
none (normoxia)
none (hypoxia)
IL-10 (normoxia)
IL-10 (hypoxia)
IFN/LPS (normoxia)
IFN/LPS (hypoxia)

FIG. 53f

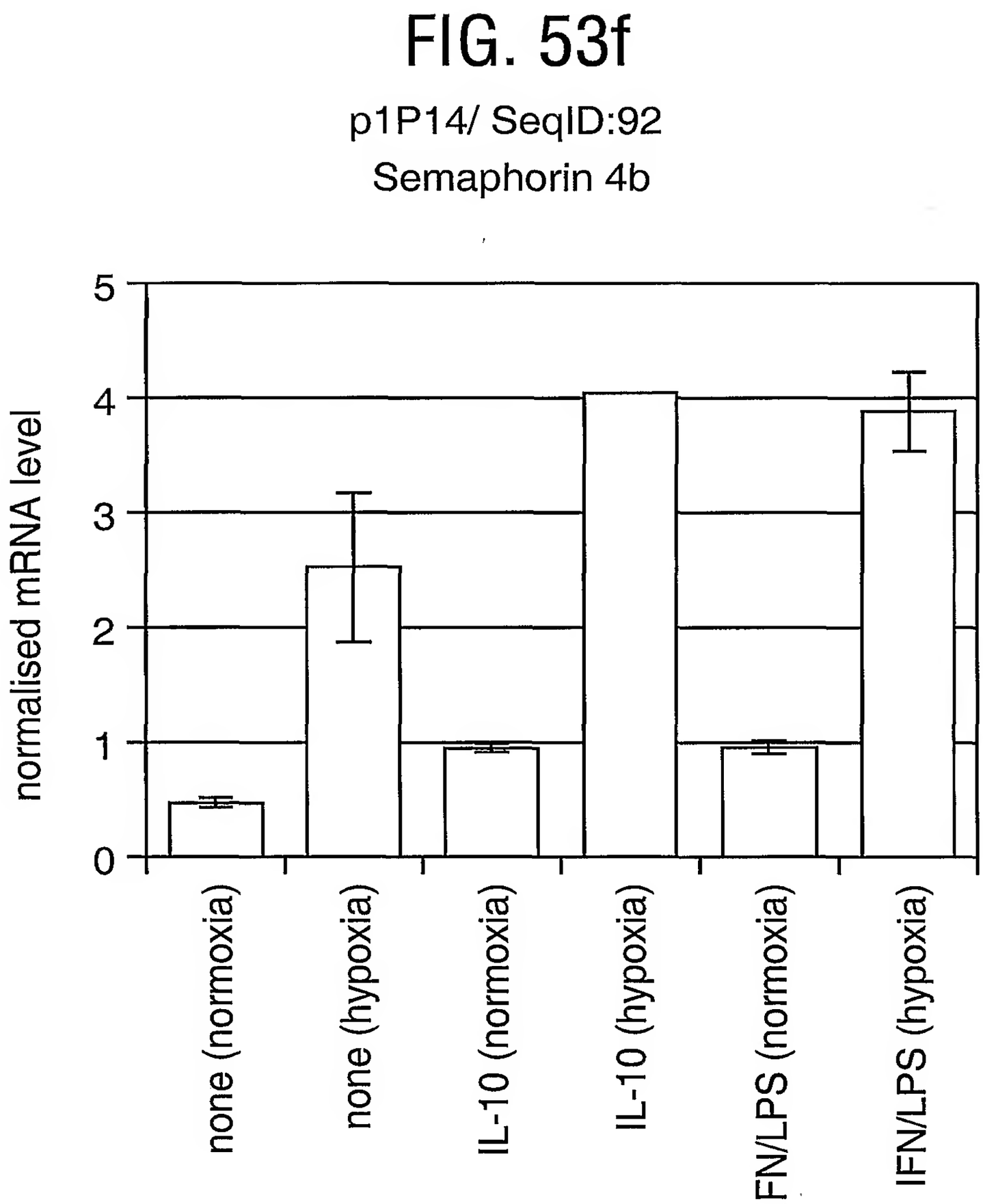

p1P14/ SeqID:92
Semaphorin 4b
normalised mRNA level
0
1
2
3
4
5
none (normoxia)
none (hypoxia)
IL-10 (normoxia)
IL-10 (hypoxia)
IFN/LPS (normoxia)
IFN/LPS (hypoxia)

FIG. 53g

p1F17/ SeqID:330

P8 protein (candidate of metastasis 1)

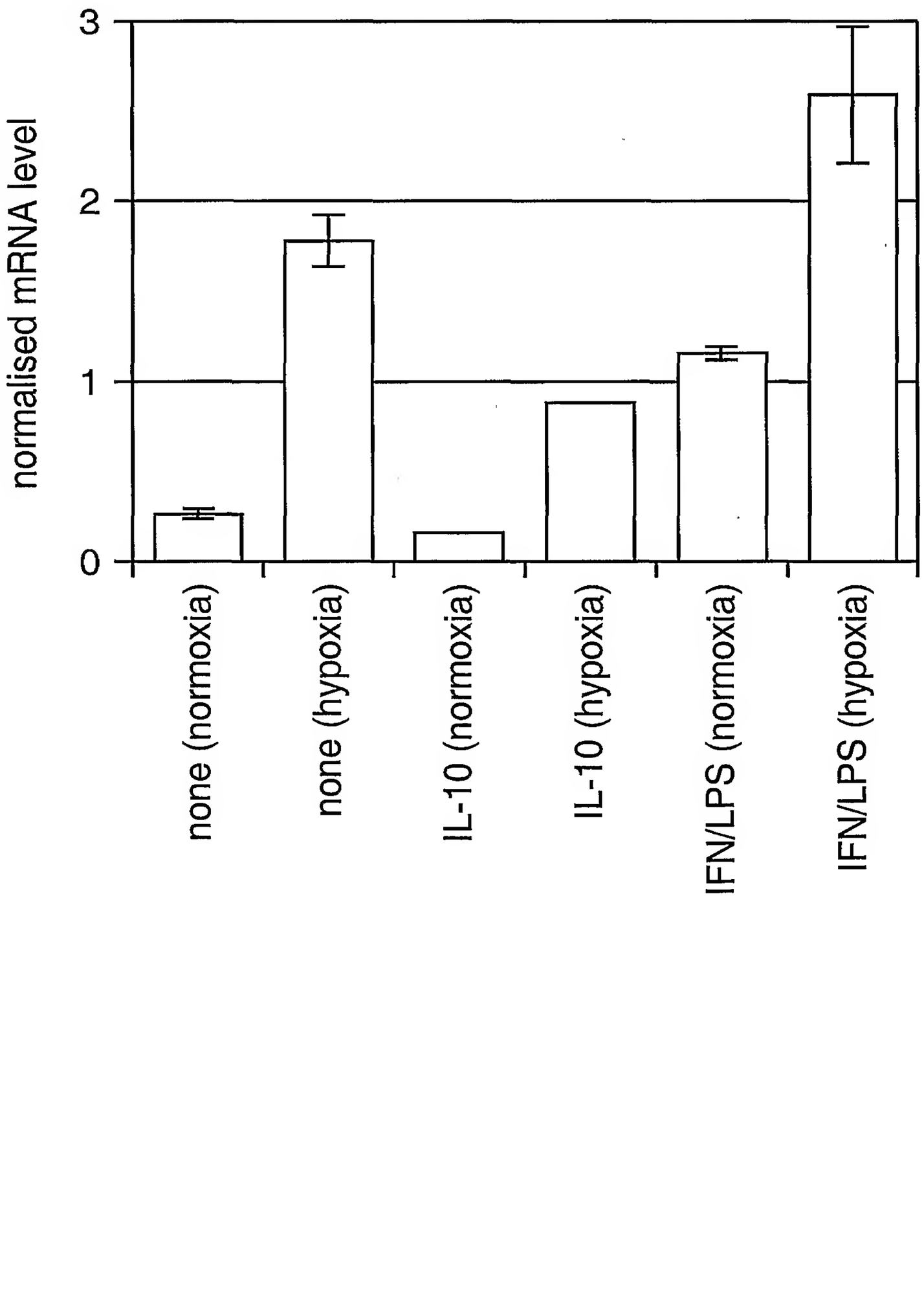


FIG. 54a

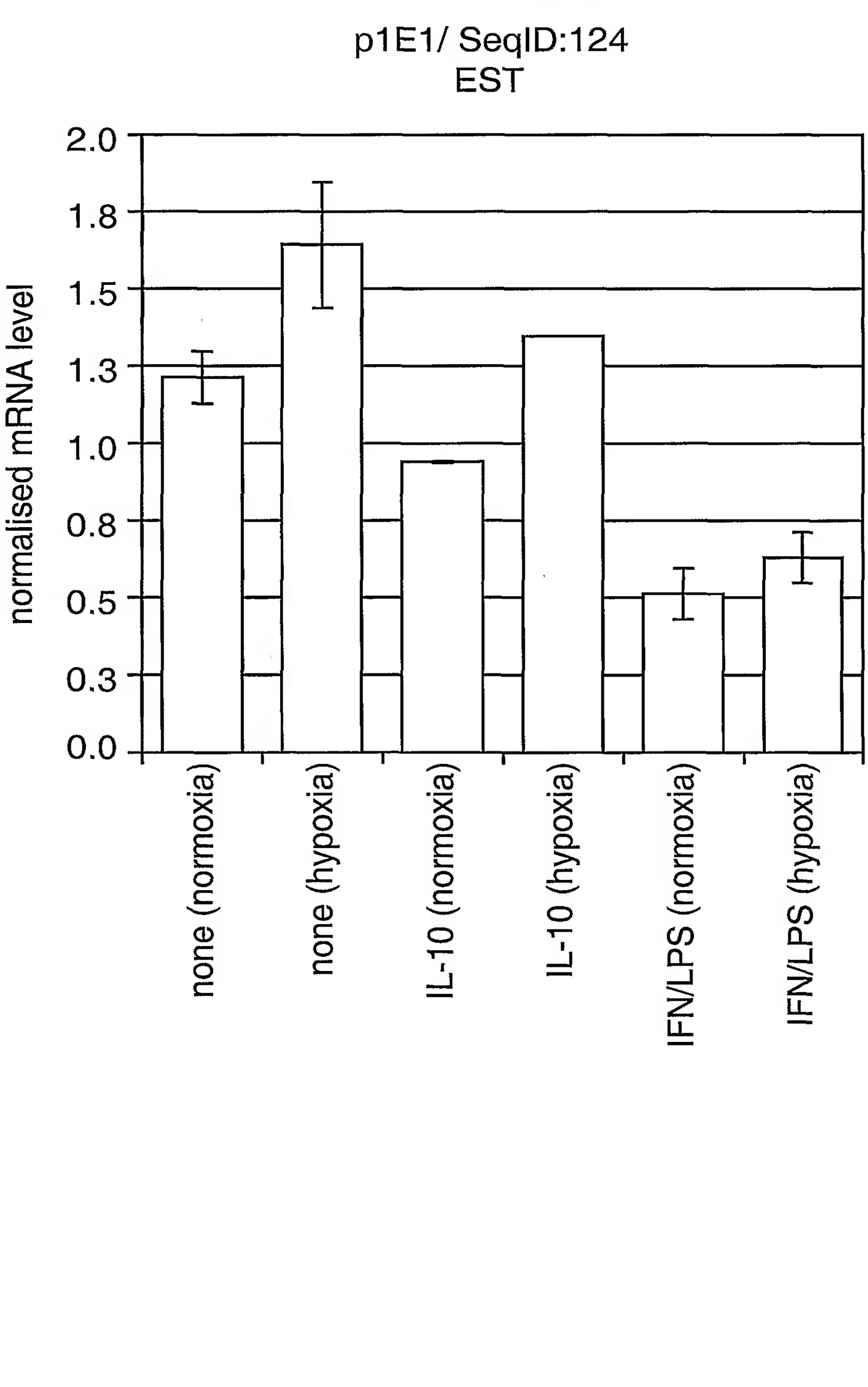

p1E1/ SeqID:124
EST
normalised mRNA level
2.0
1.8
1.5
1.3
1.0
0.8
0.5
0.3
0.0
none (normoxia)
none (hypoxia)
IL-10 (normoxia)
IL-10 (hypoxia)
IFN/LPS (normoxia)
IFN/LPS (hypoxia)

FIG. 54b

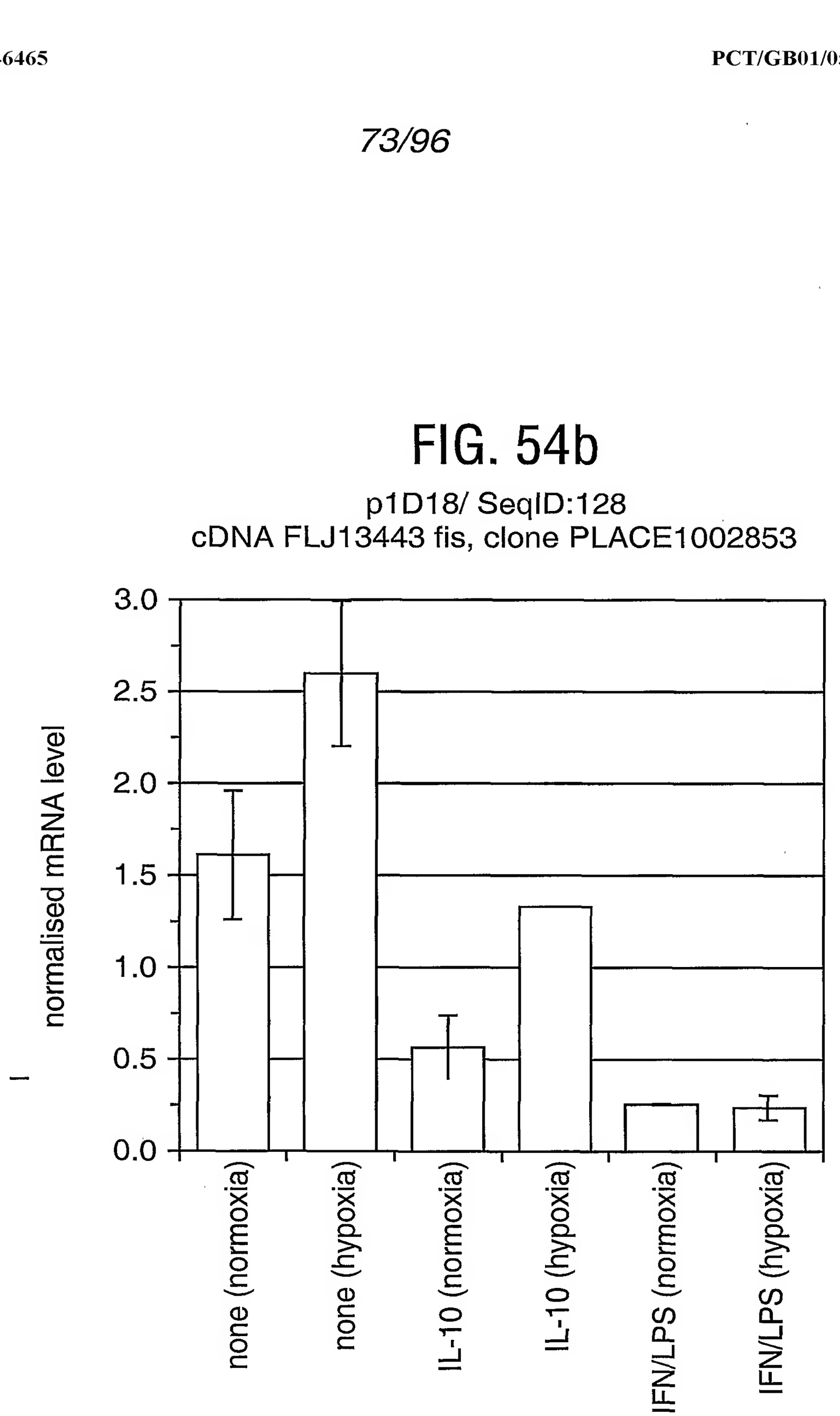

p1D18/ SeqID:128
cDNA FLJ13443 fis, clone PLACE1002853
normalised mRNA level
3.0
2.5
2.0
1.5
1.0
0.5
0.0
none (normoxia)
none (hypoxia)
IL-10 (normoxia)
IL-10 (hypoxia)
IFN/LPS (normoxia)
IFN/LPS (hypoxia)

FIG. 54c

p1F9/ SeqID:20

Hypothetical protein KIAA0742

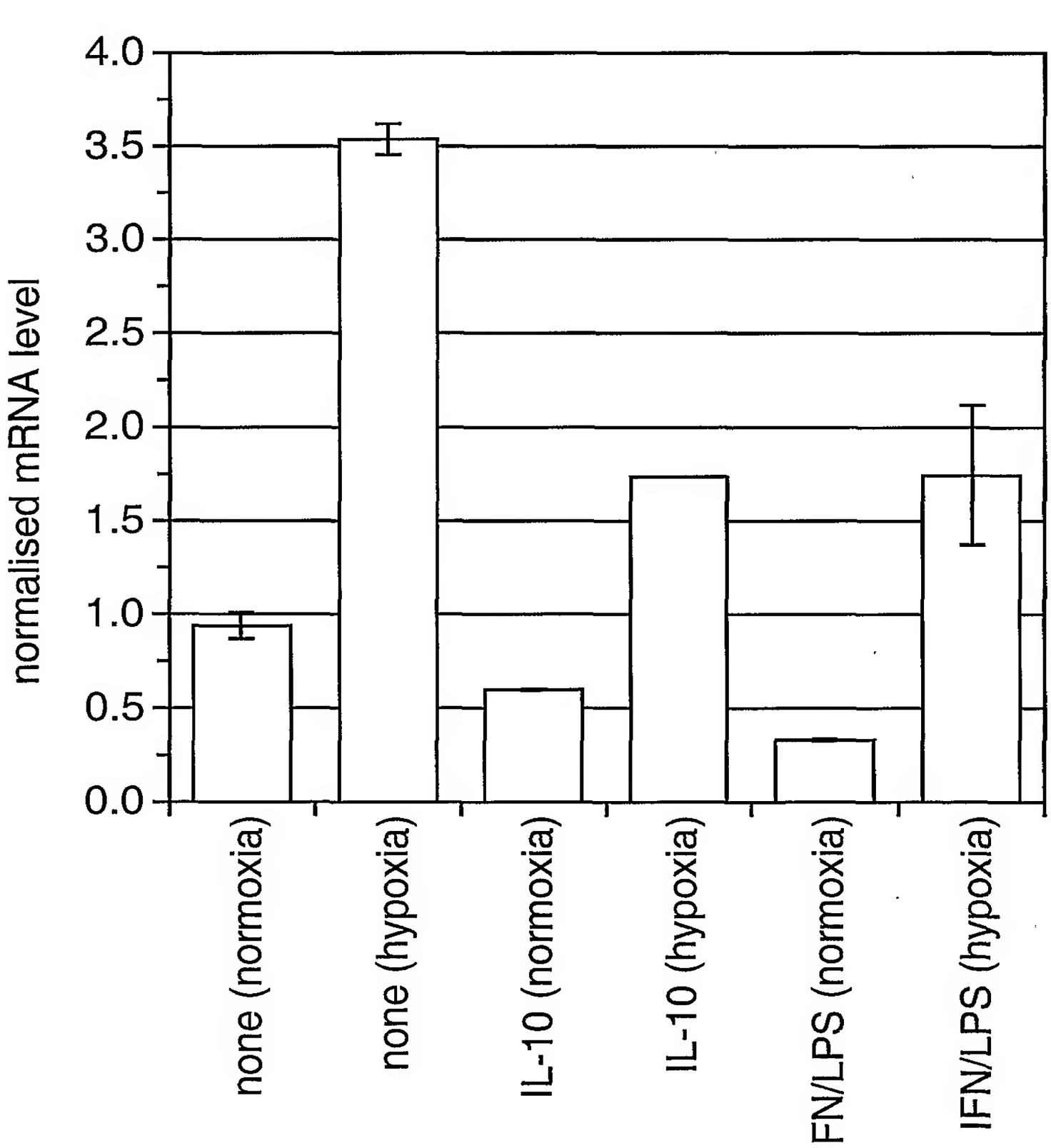


FIG. 54d

p1D1/ SeqID:24

Hypothetical protein FLJ10134

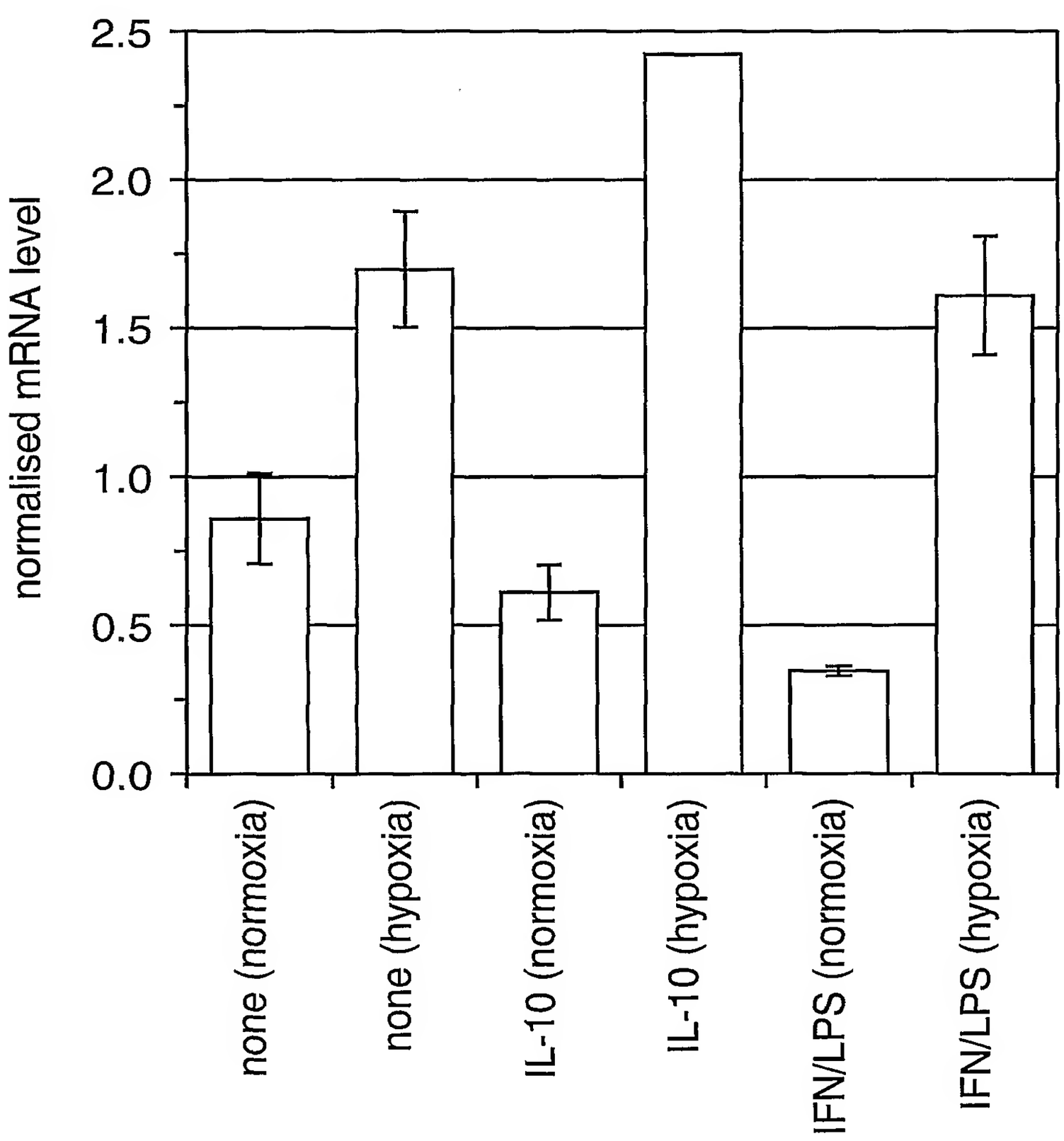


FIG. 54e

p1F8/ SeqID:10
Hypothetical protein KIAA0914

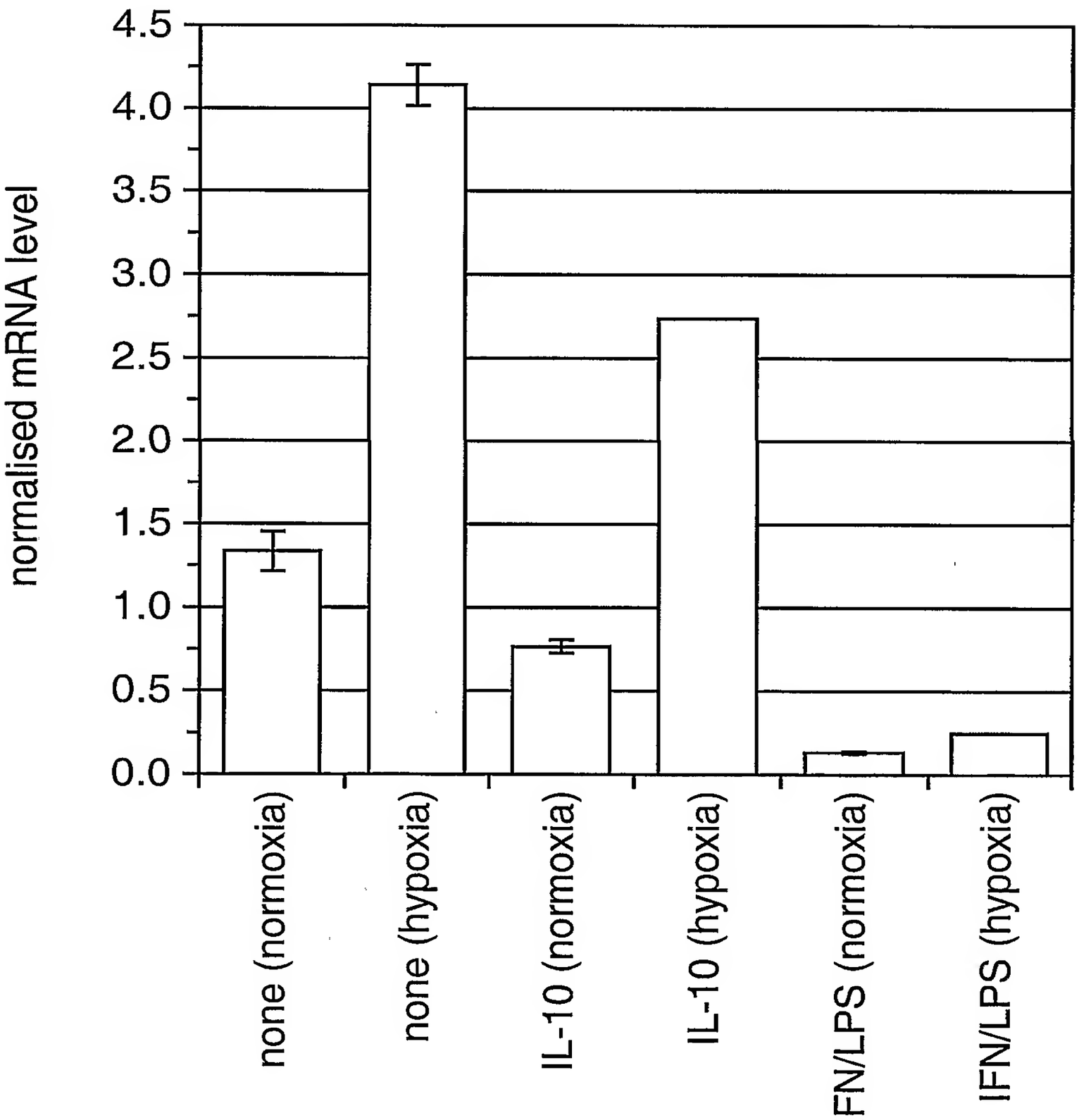


FIG. 54f

p1D16/ SeqID:34

Hypothetical protein FLJ20308

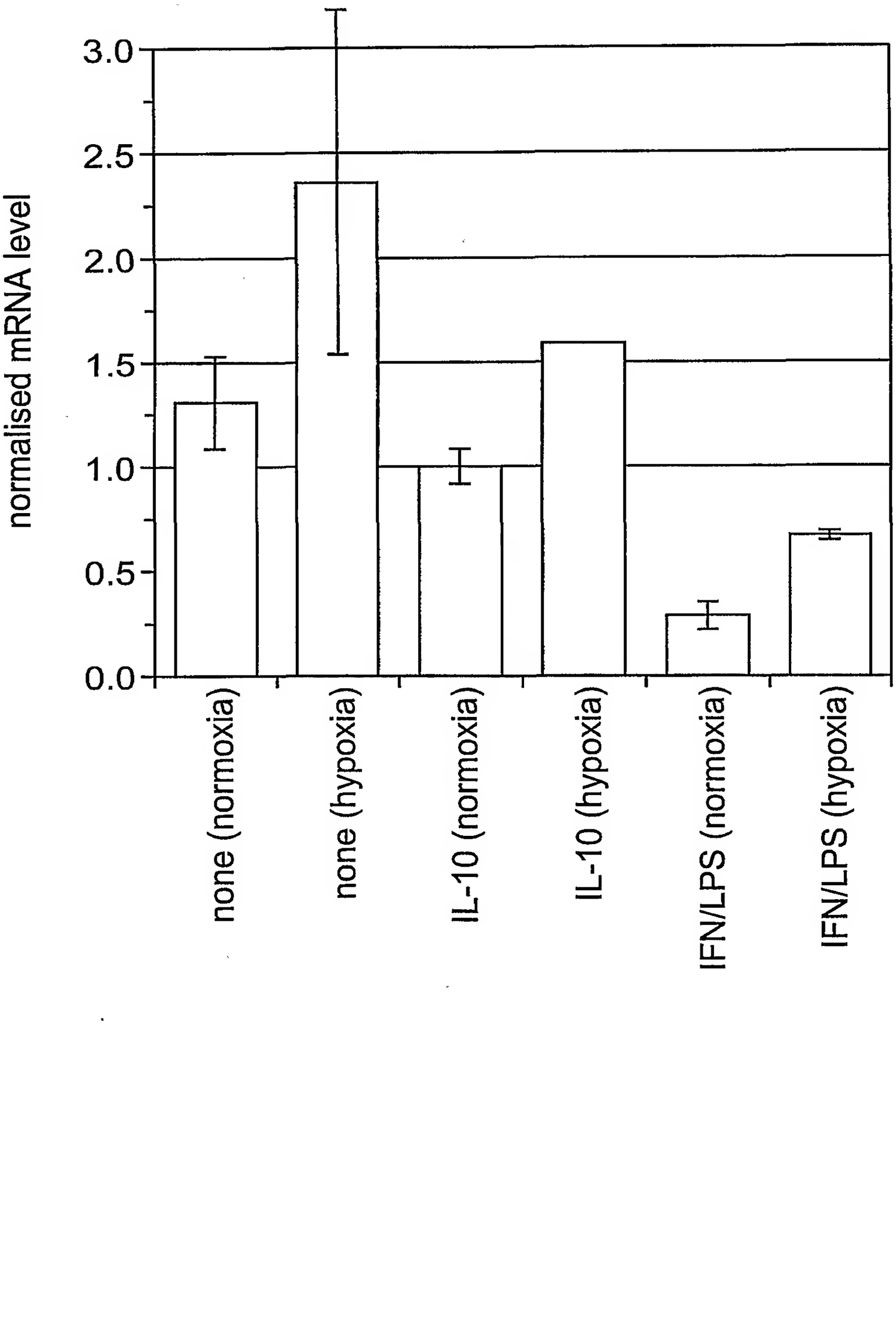


FIG. 54g

p1F3/ SeqID:334
Hypothetical protein XP_017131

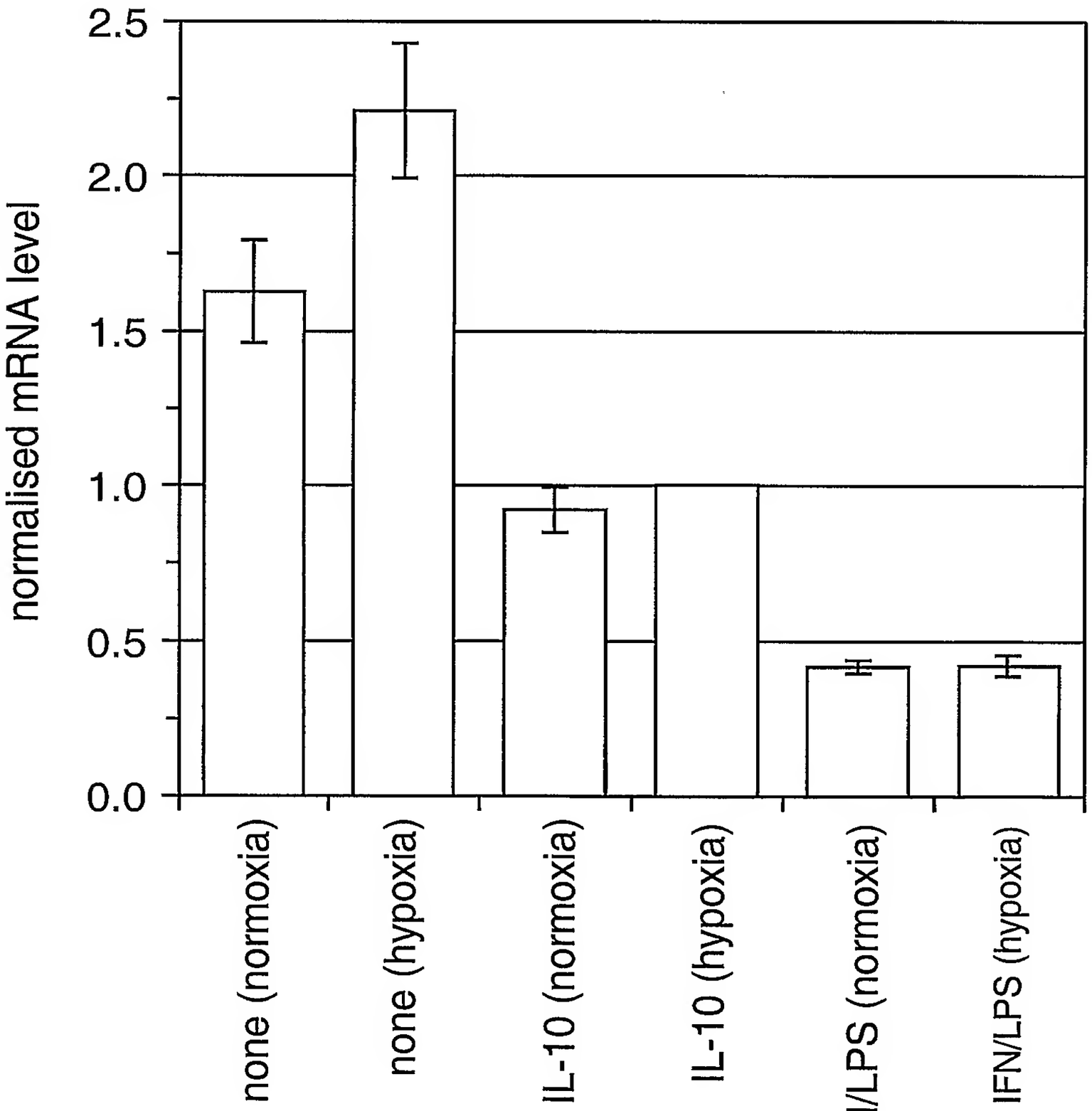


FIG. 54h

p1D12/ SeqID:30

Hypothetical protein KIAA1376

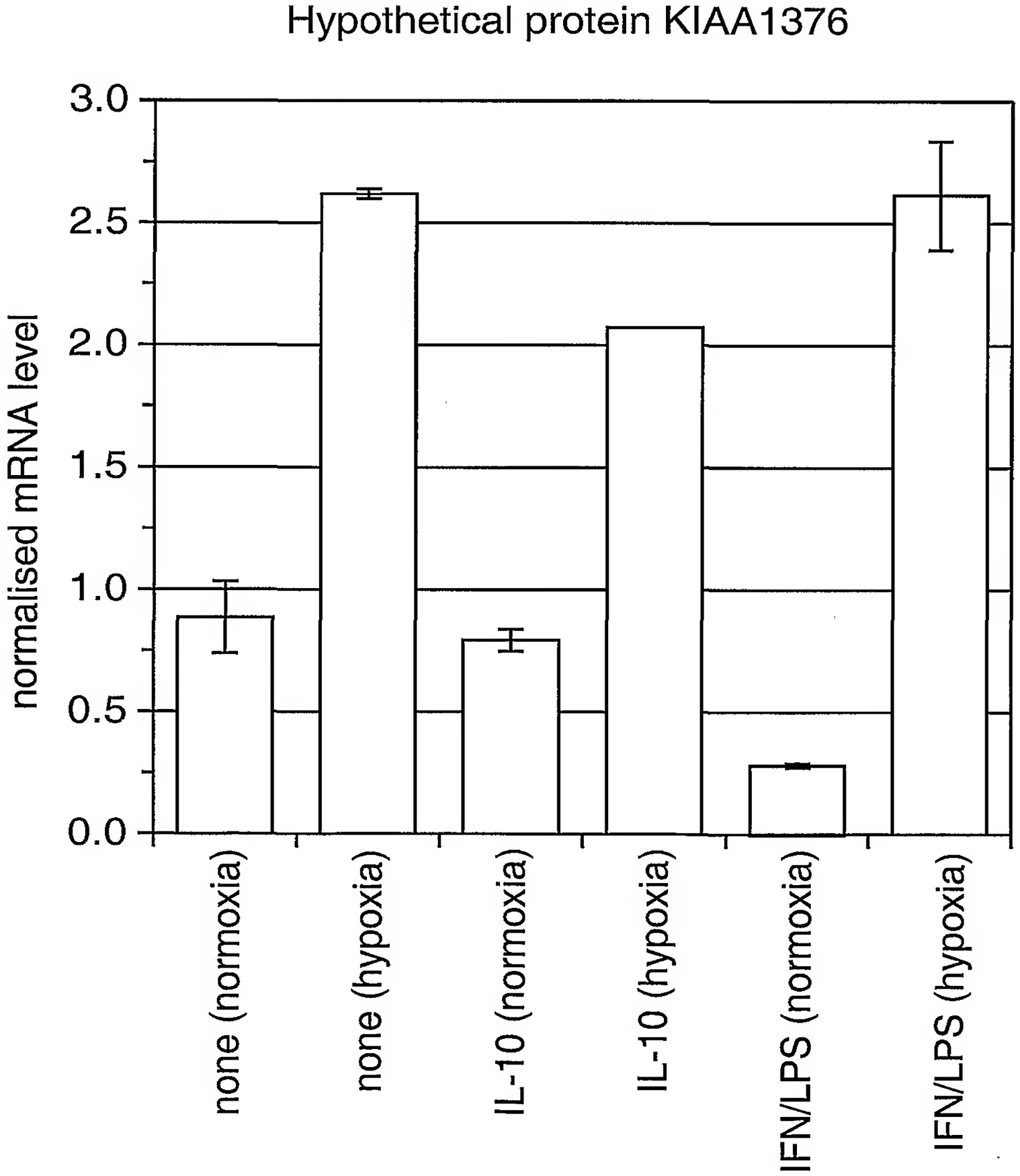


FIG. 55a

p1D9/ SeqID:28

Hypothetical protein DKFZP564D116

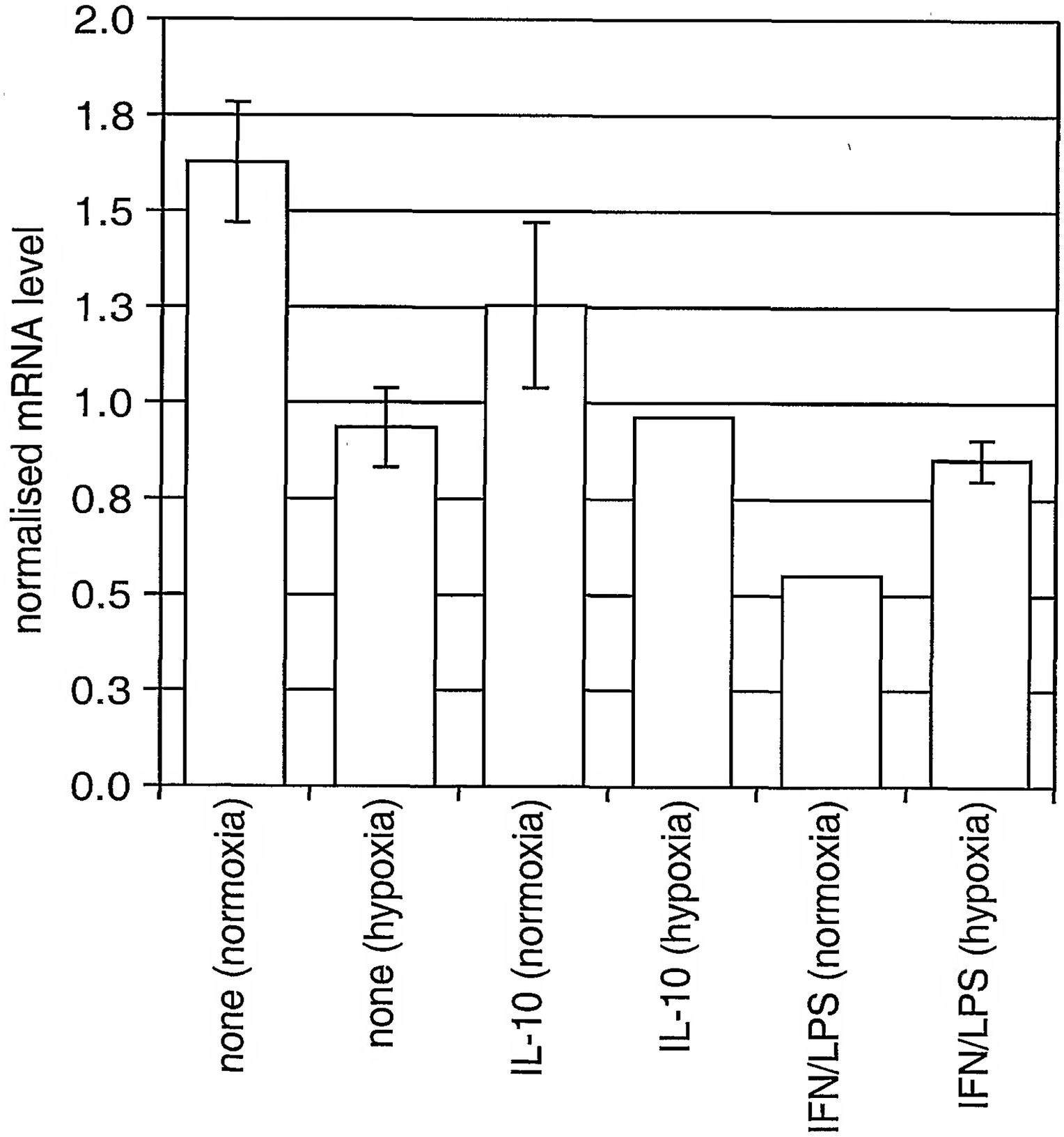


FIG. 55b

p1l15/ SeqID:48

Hypothetical protein CGI-117

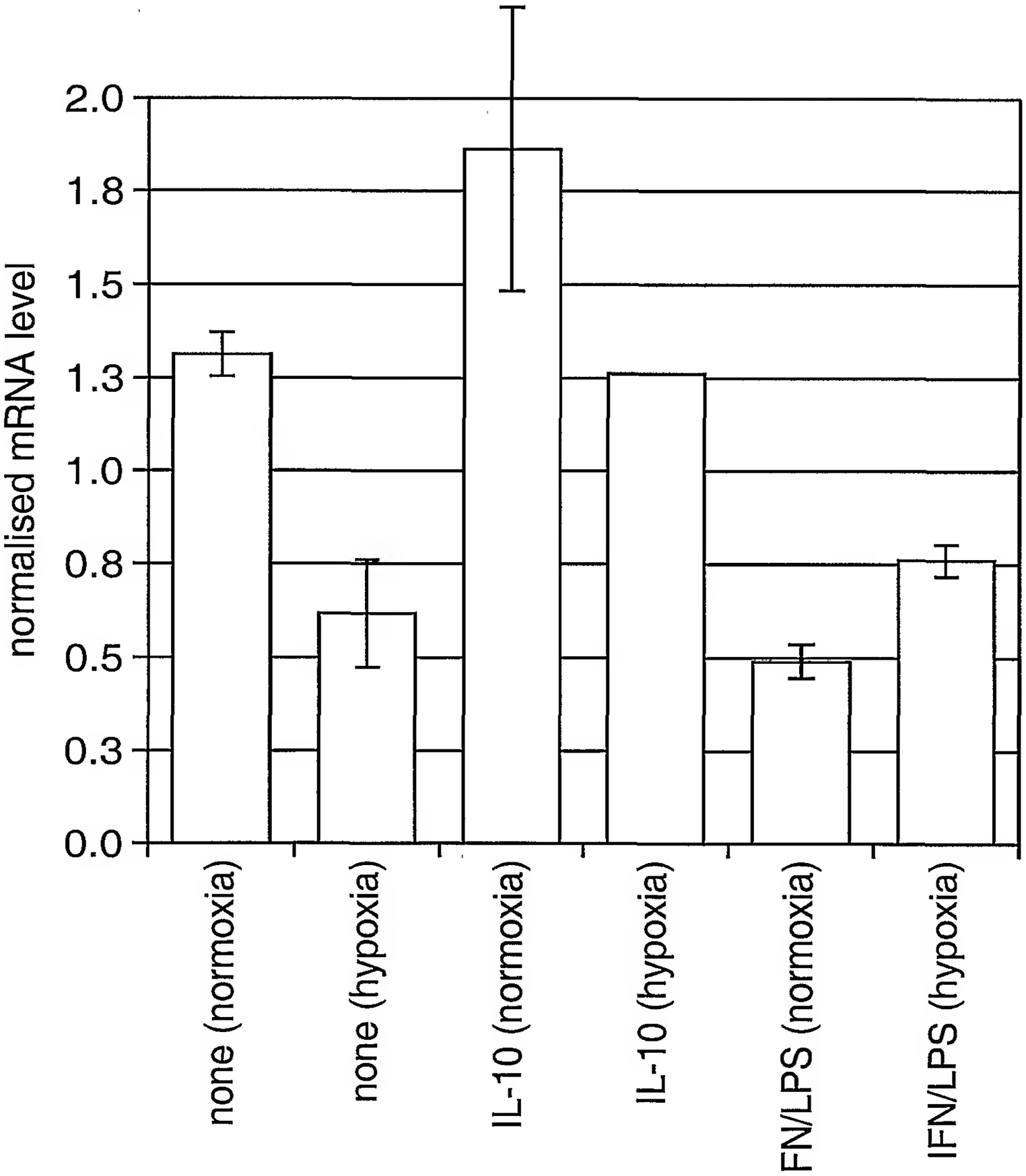


FIG. 55c

p1I4/ SeqID:54

Hypothetical protein HSPC196

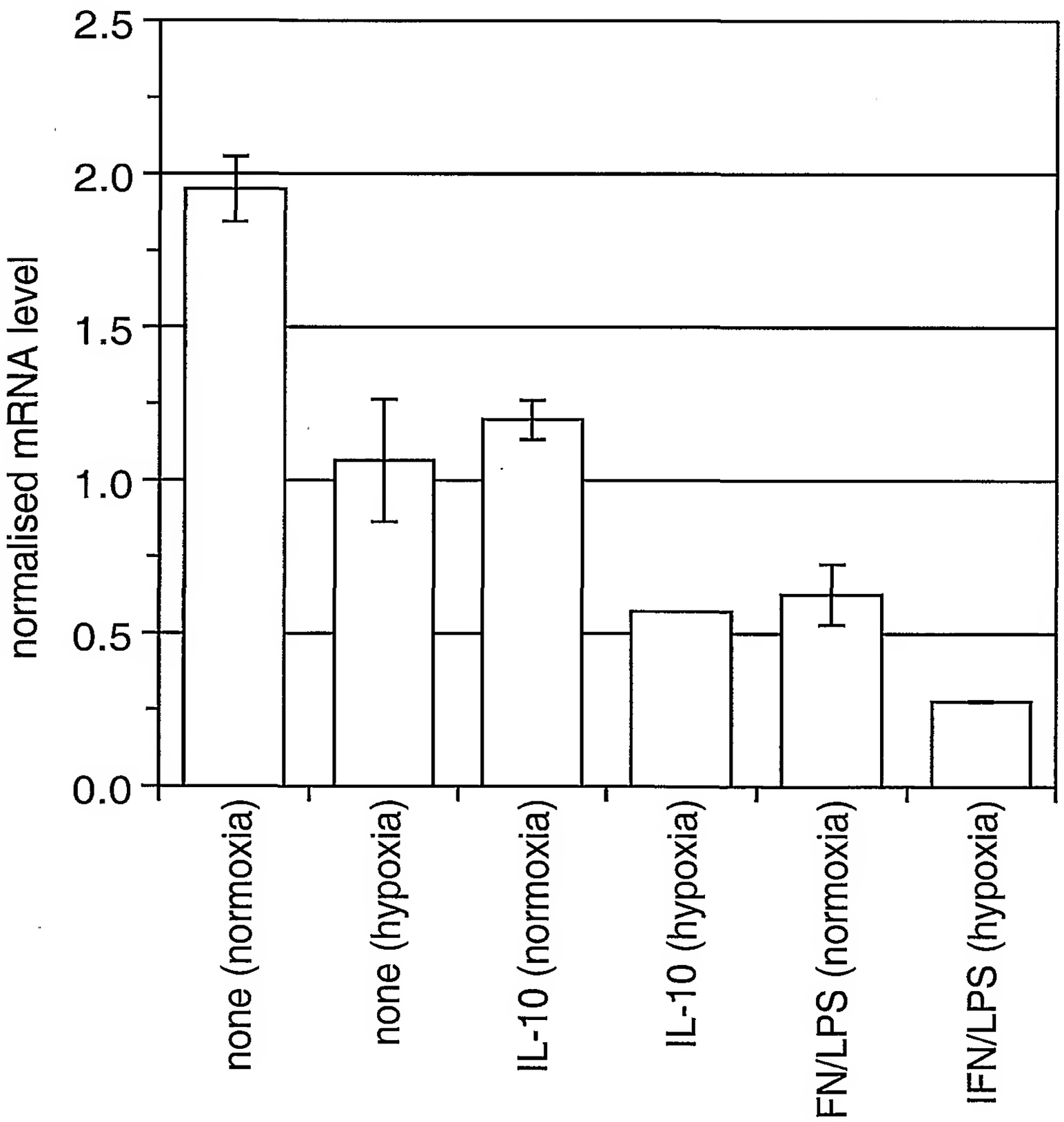


FIG. 55d

p1E13/ SeqID:22

Hypothetical protein PRO0823

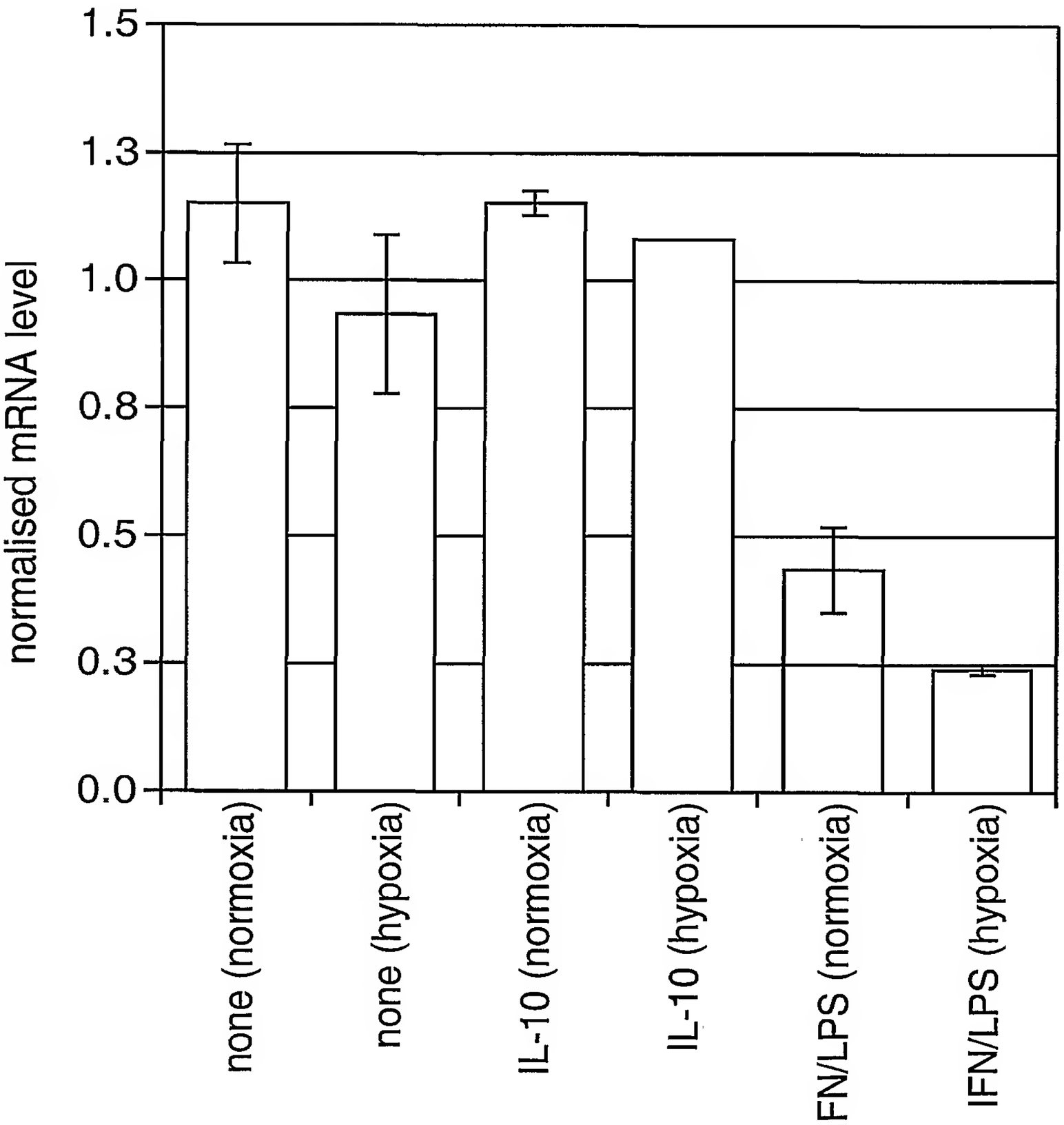


FIG. 55e

p1F10/ SeqID:6
Hypothetical protein DKFZp434P0116

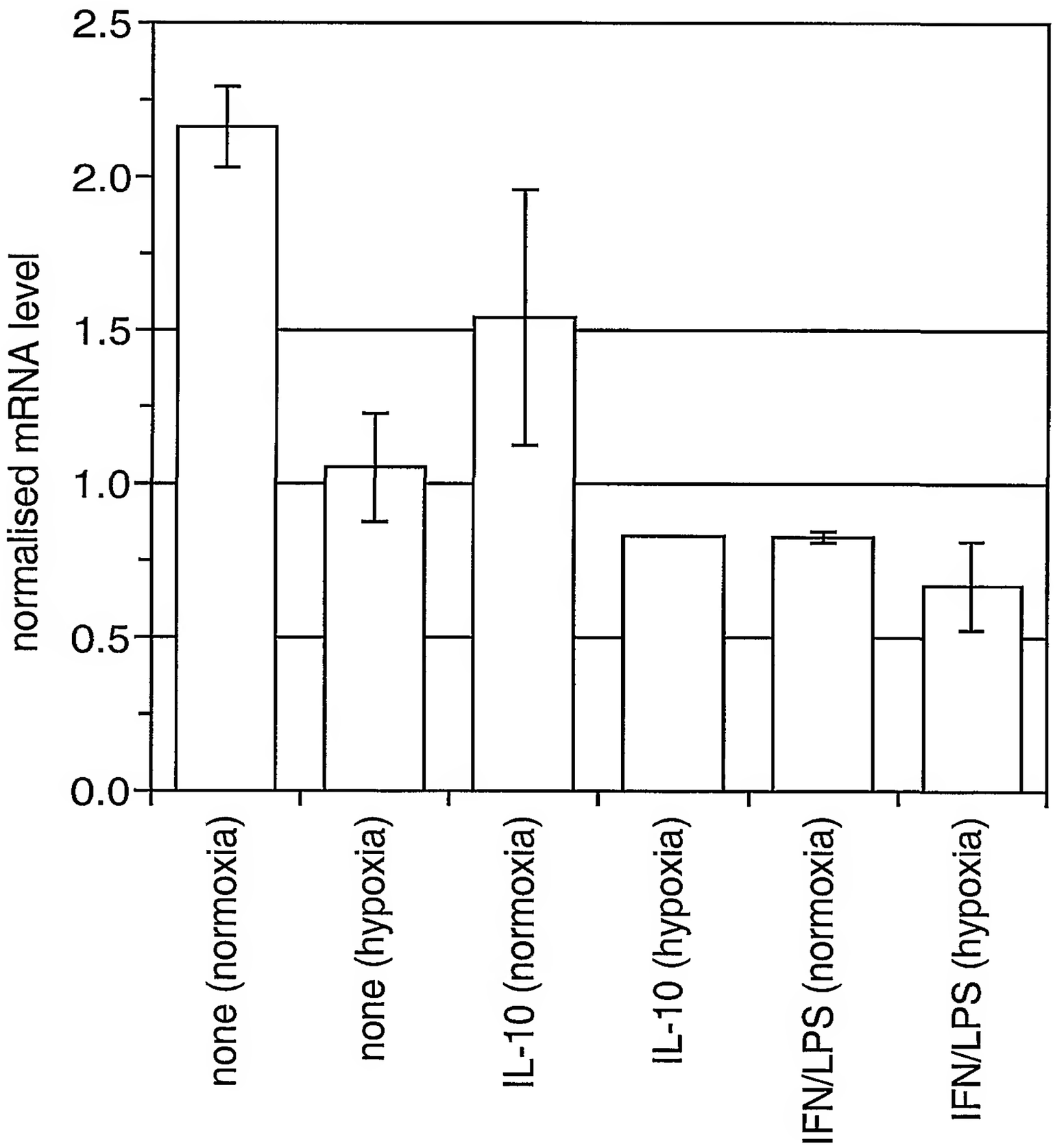


FIG. 55f

p1l2/ SeqID:150

cDNA FLJ11302 fis, clone PLACE1009971

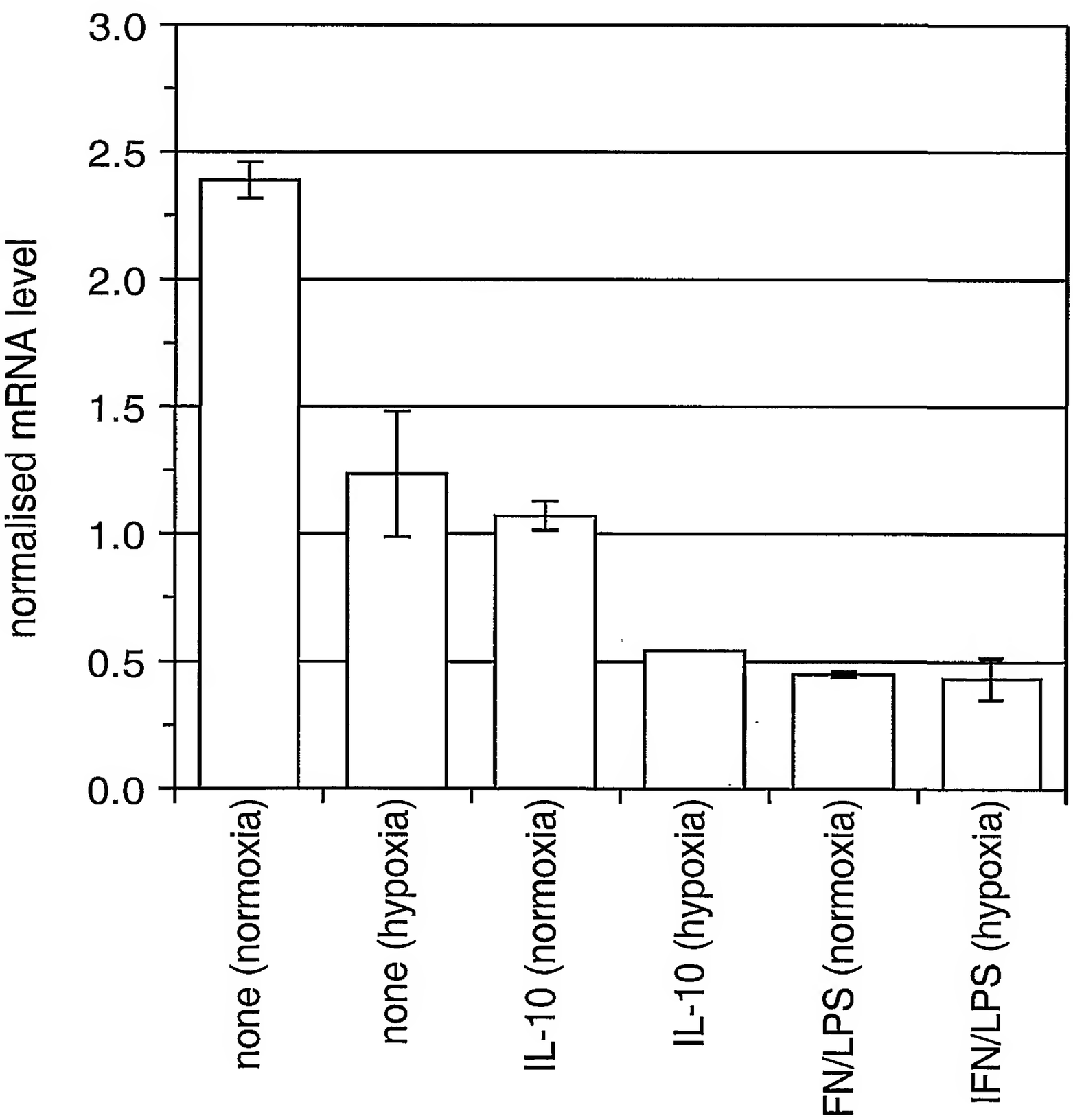


FIG. 55g

p1I5/ SeqID:42
Hypothetical protein FLJ10815

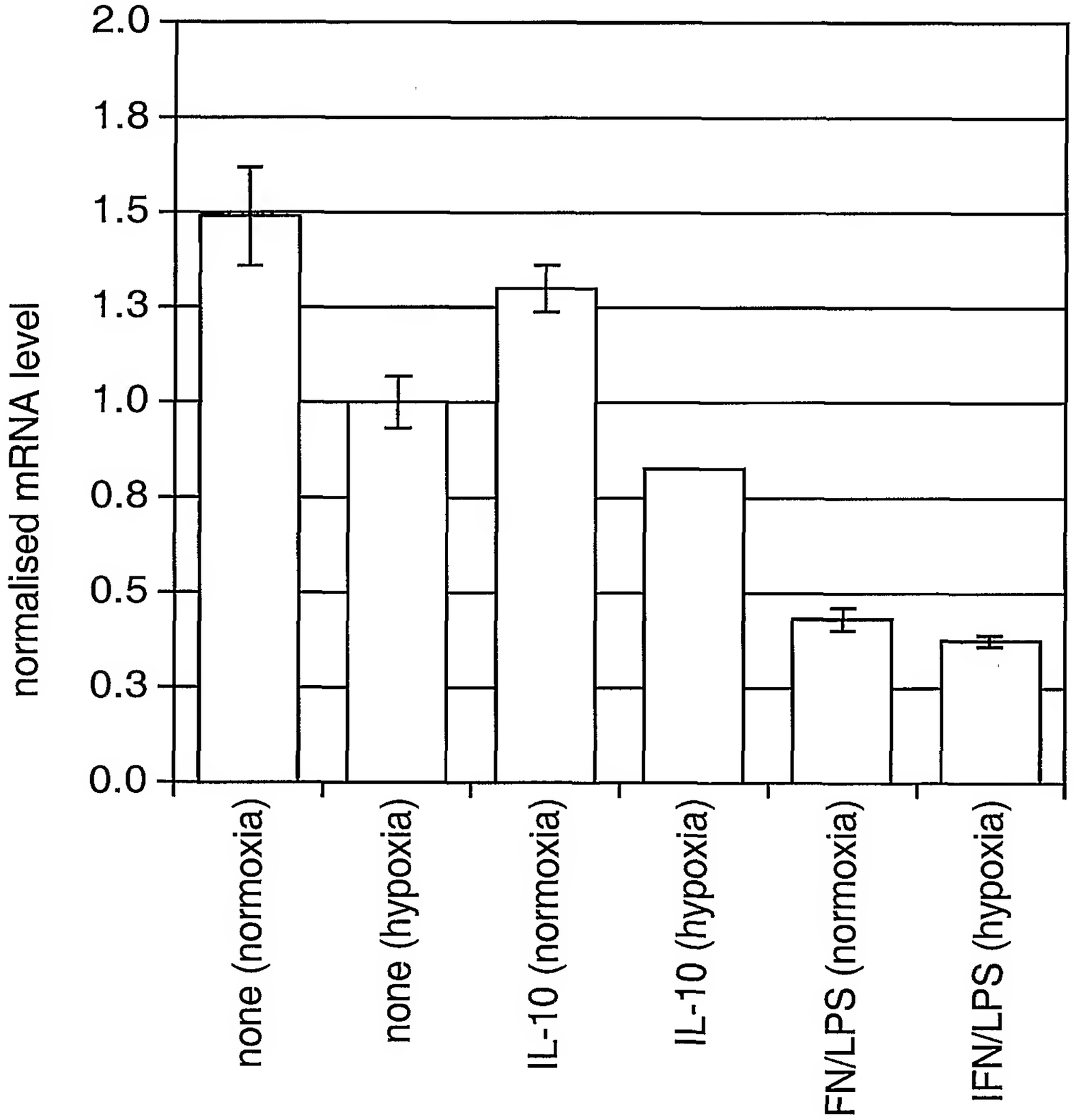


FIG. 55h

p1G20/ SeqID:204

cDNA YO23H03

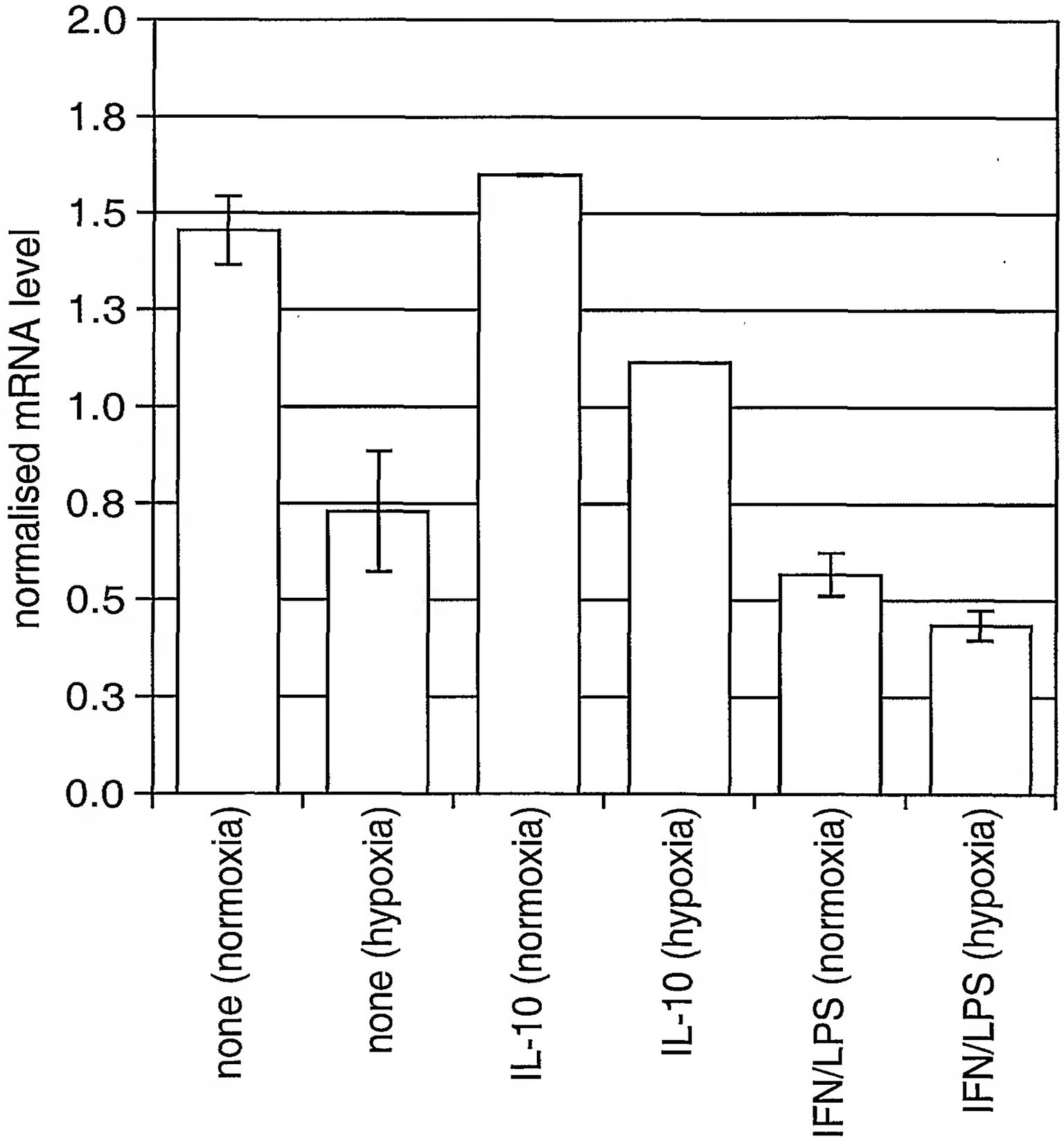


FIG. 56a

p1G5/ SeqID:280
MAX-interacting protein 1

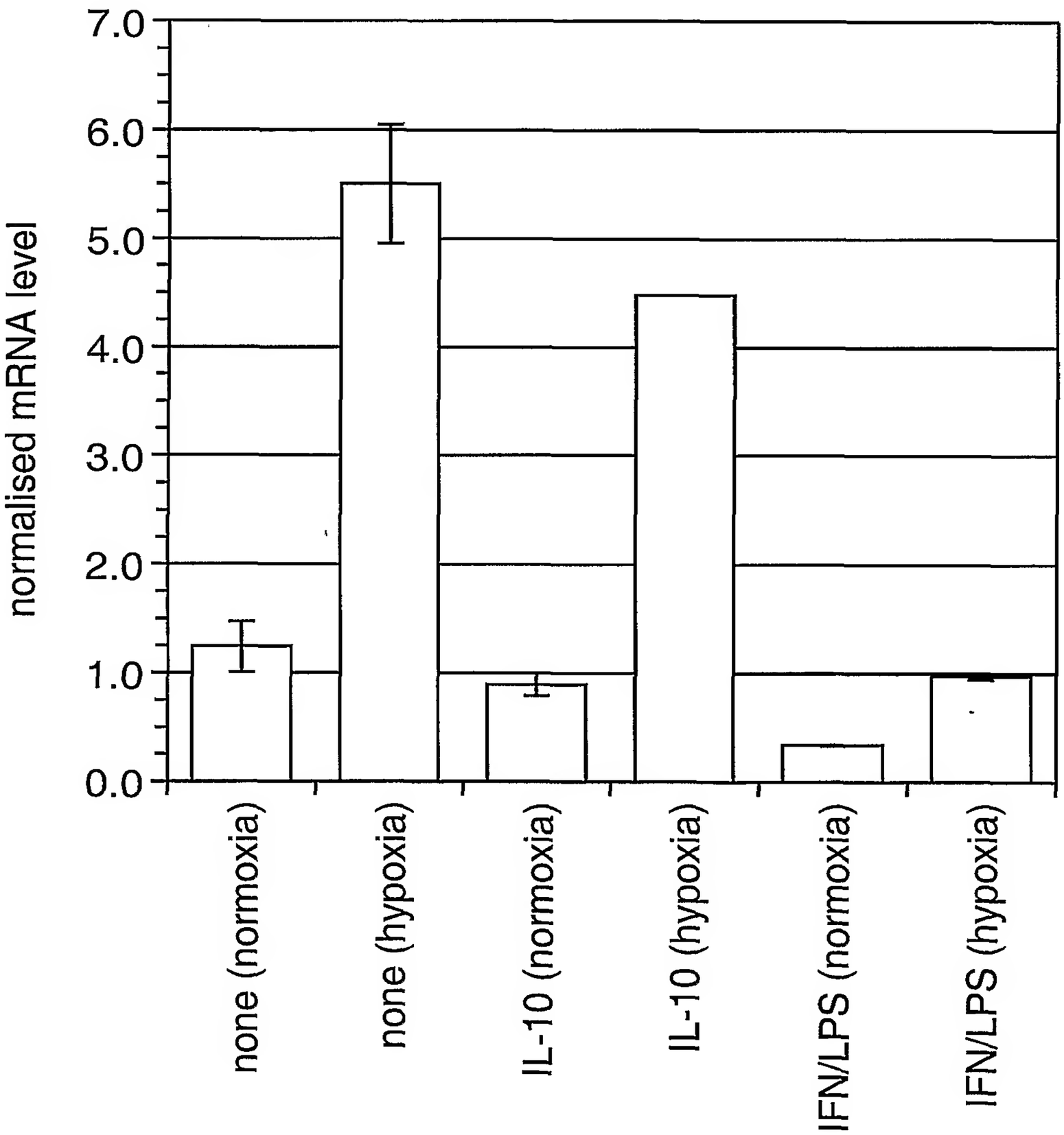


FIG. 56b

p1D22/ SeqID:120

MAX-interacting protein 1

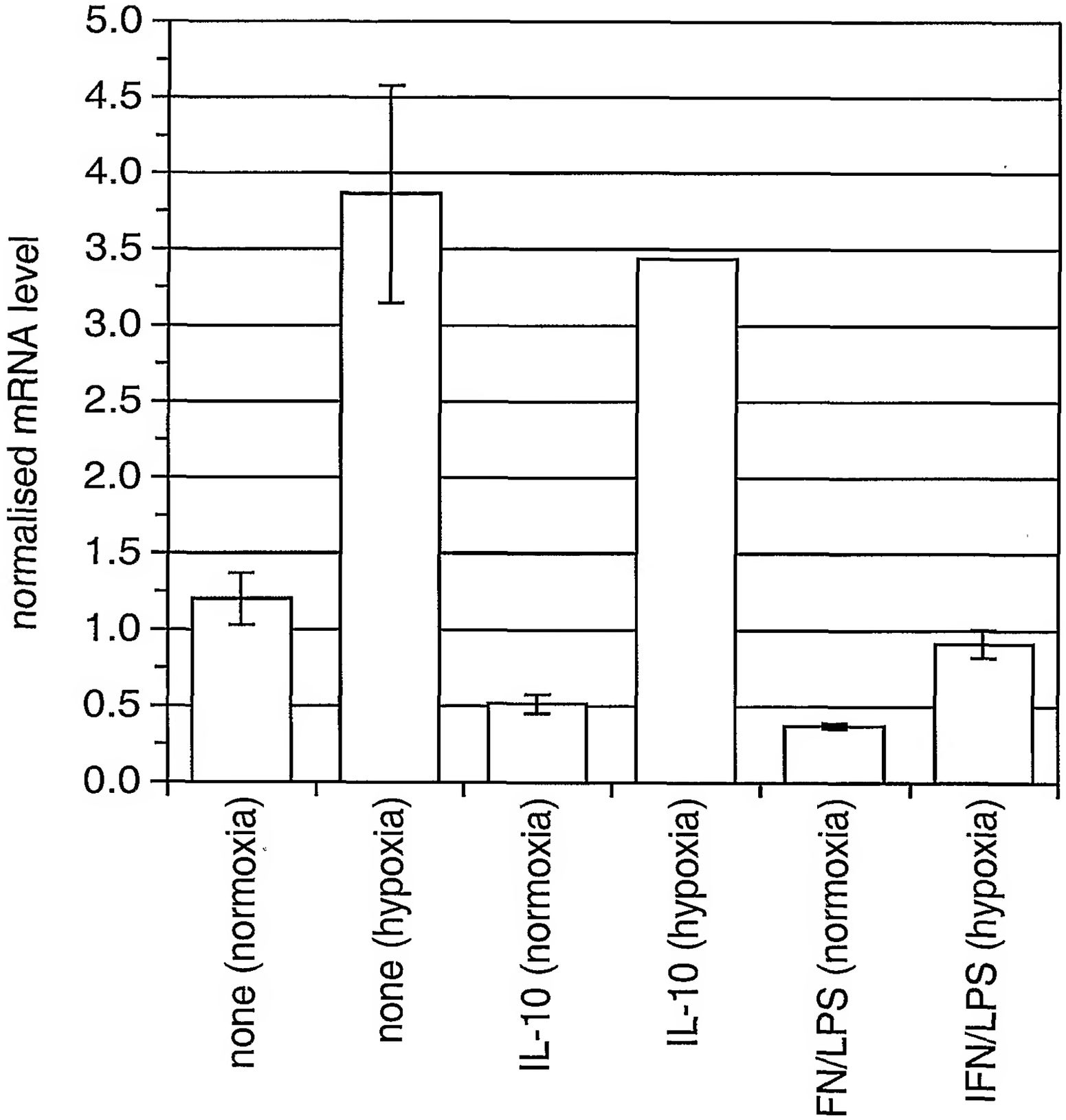


FIG. 56c

p1G17/ SeqID:316

Early development regulator 2

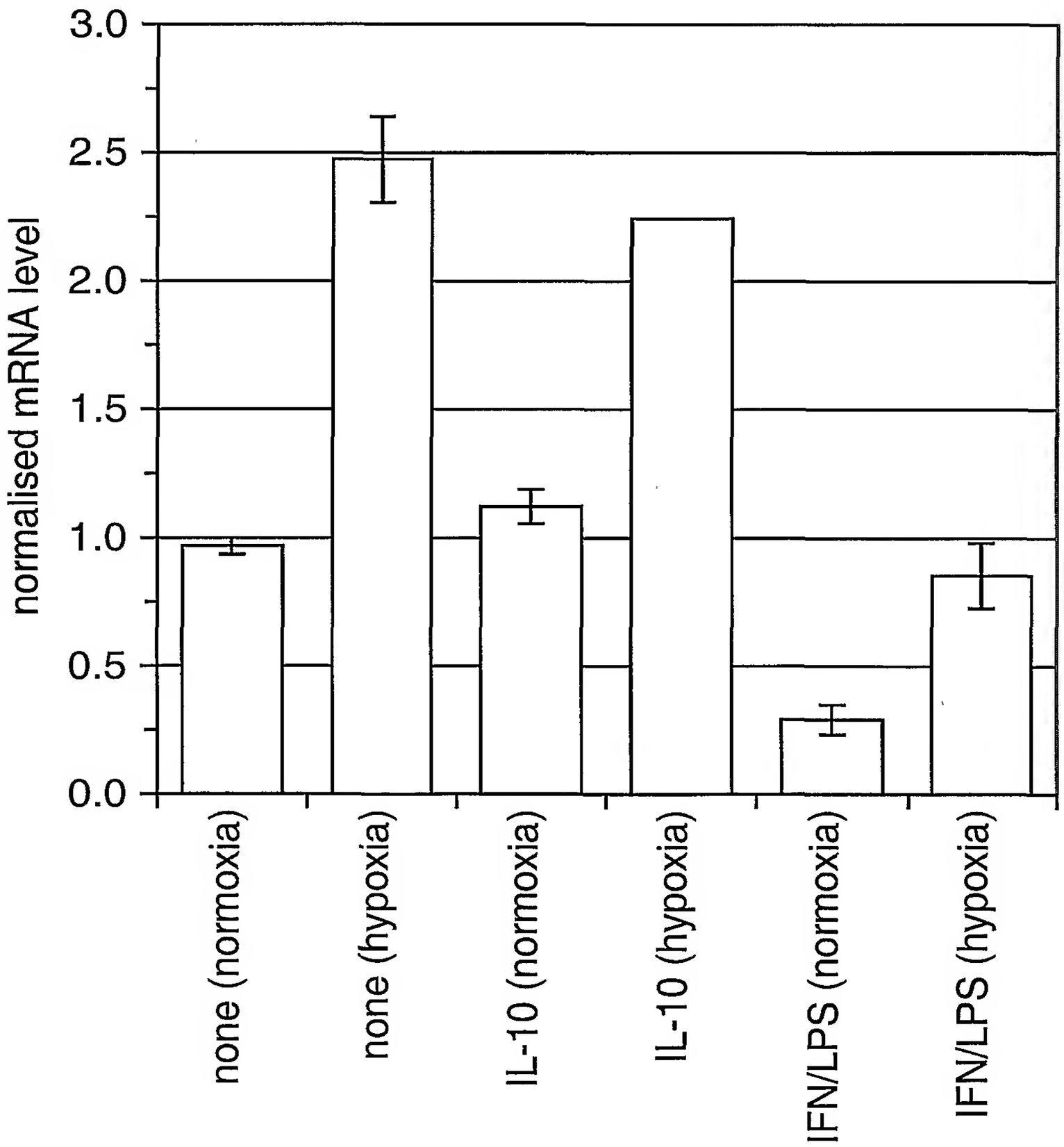


FIG. 56d

p1G9/ SeqID:306

PI-3-kinase, catalytic, beta polypeptide

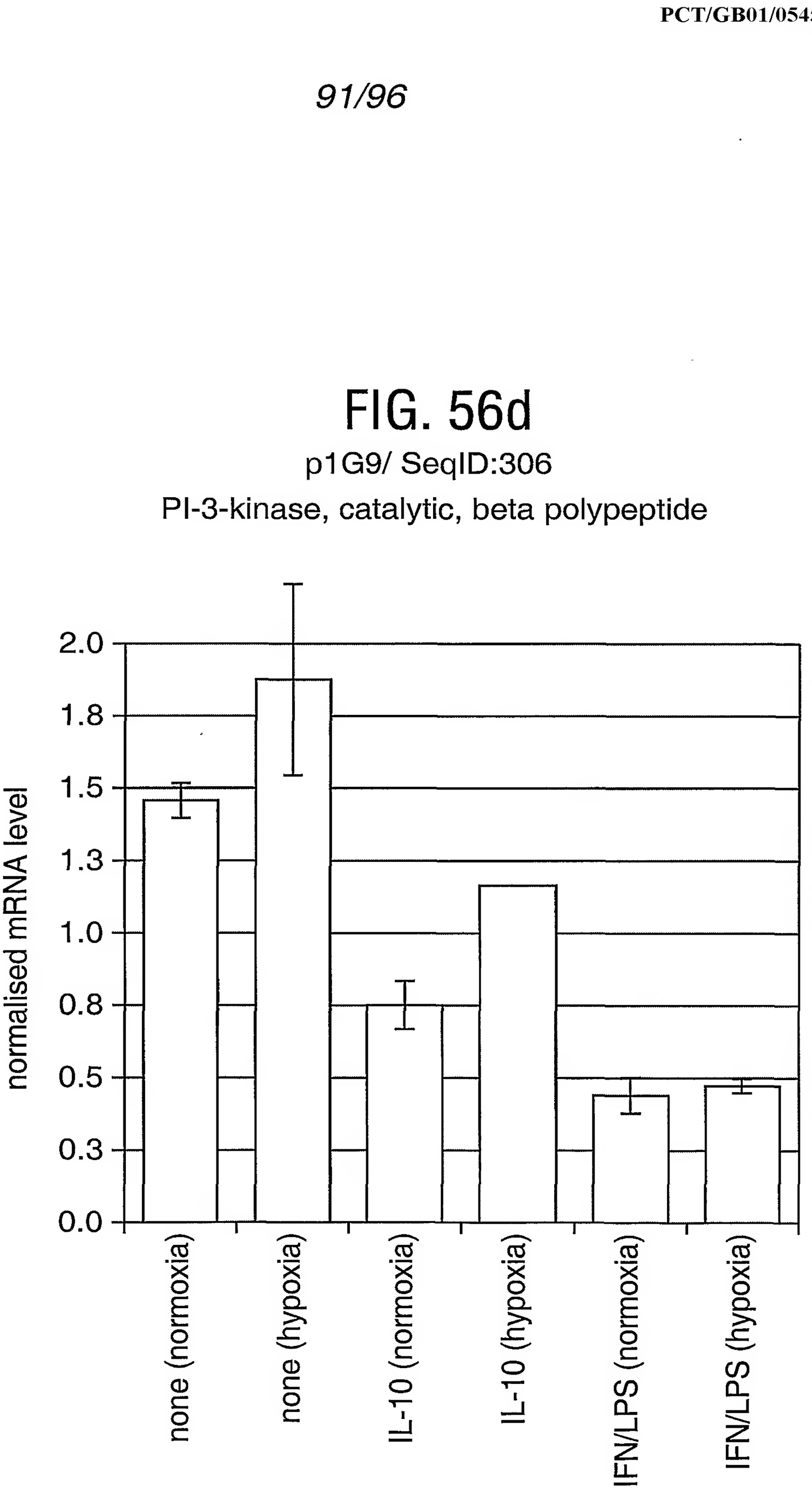


FIG. 56e

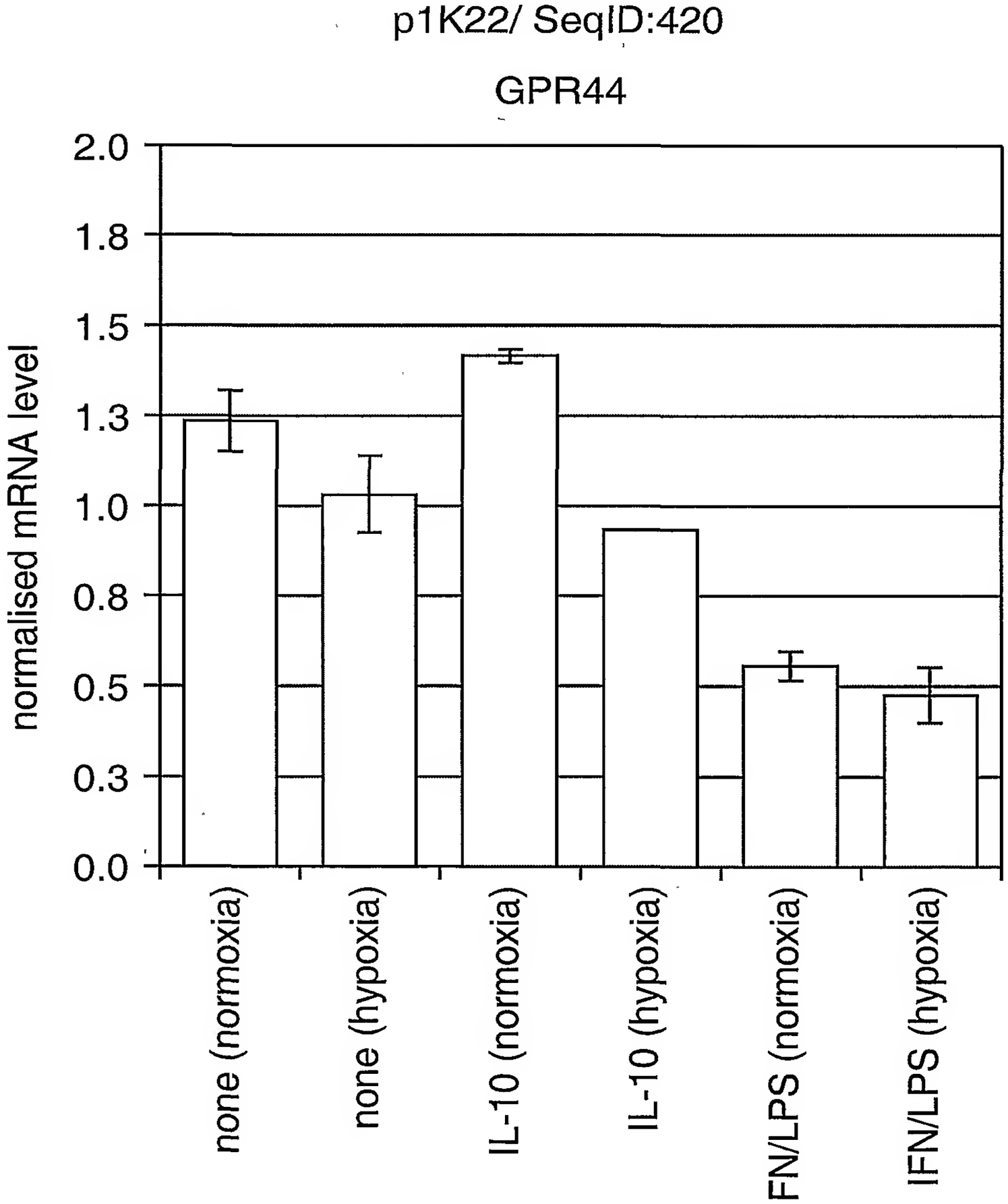

p1K22/ SeqID:420
GPR44
normalised mRNA level
2.0
1.8
1.5
1.3
1.0
0.8
0.5
0.3
0.0
none (normoxia)
none (hypoxia)
IL-10 (normoxia)
IL-10 (hypoxia)
IFN/LPS (normoxia)
IFN/LPS (hypoxia)

FIG. 56f

p1C10/ SeqID:376

Regulator of G-protein signalling 1

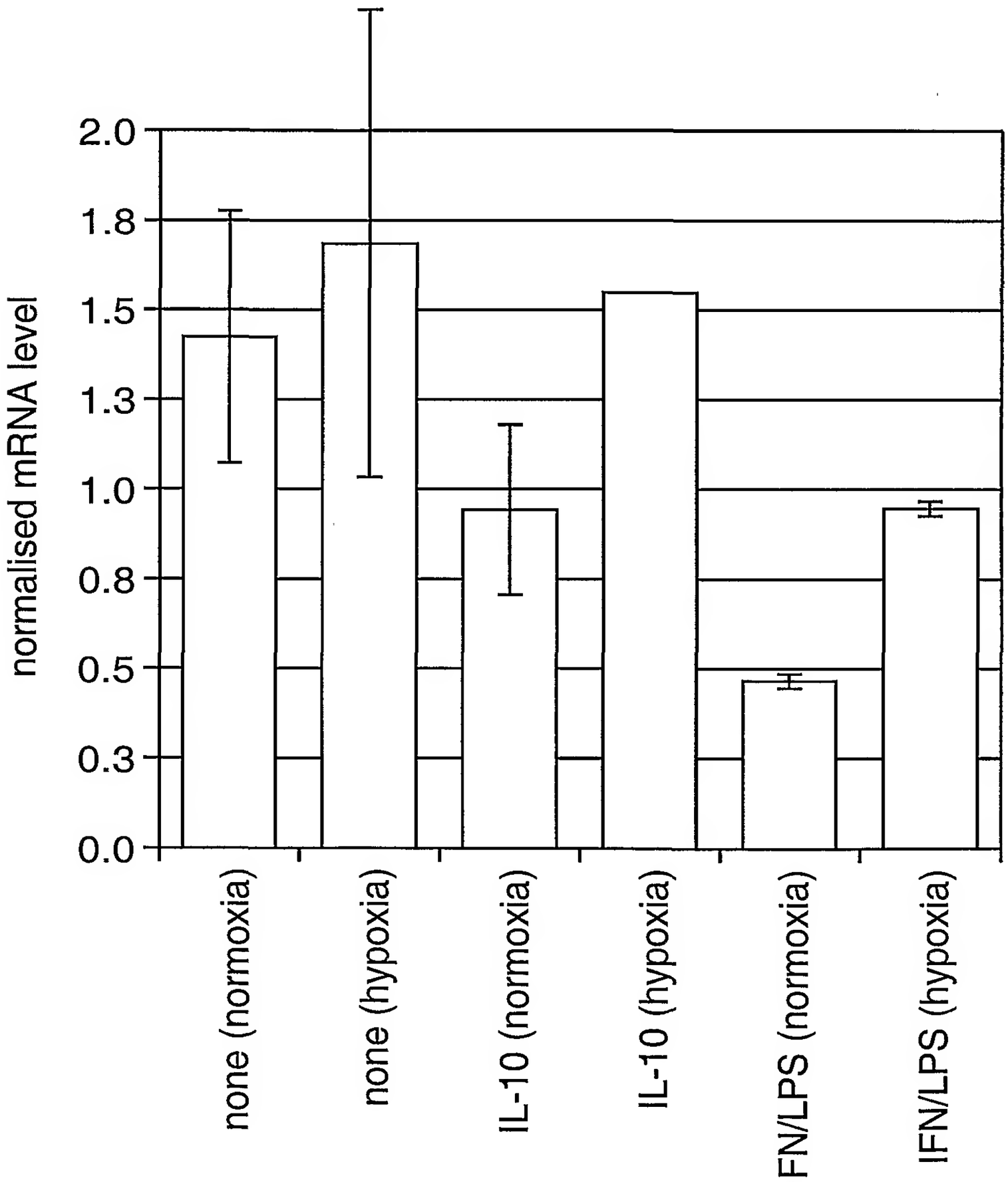


FIG. 56g

p1D6/ SeqID:68

ERO1 (S. cerevisiae)-like

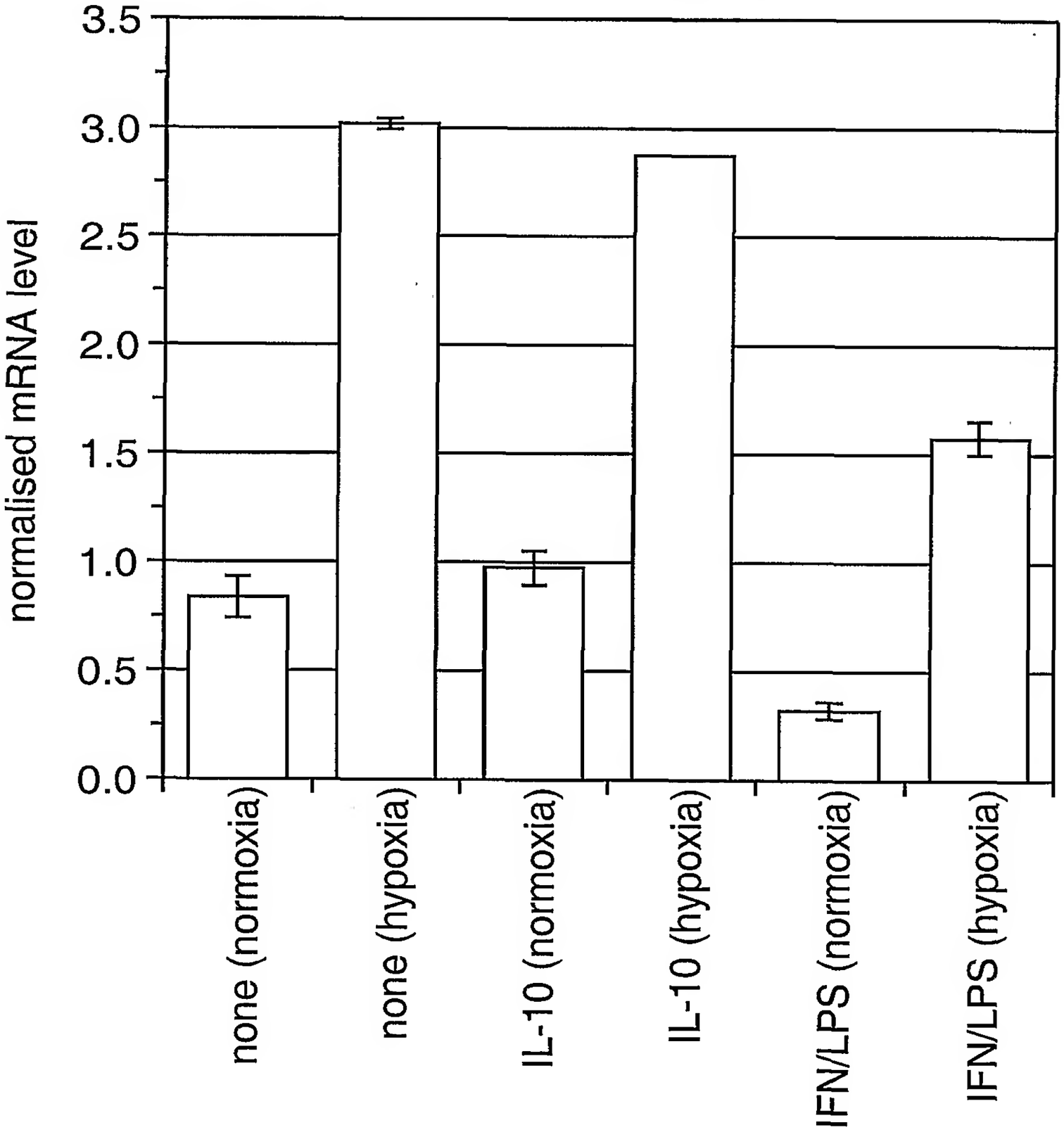


FIG. 57

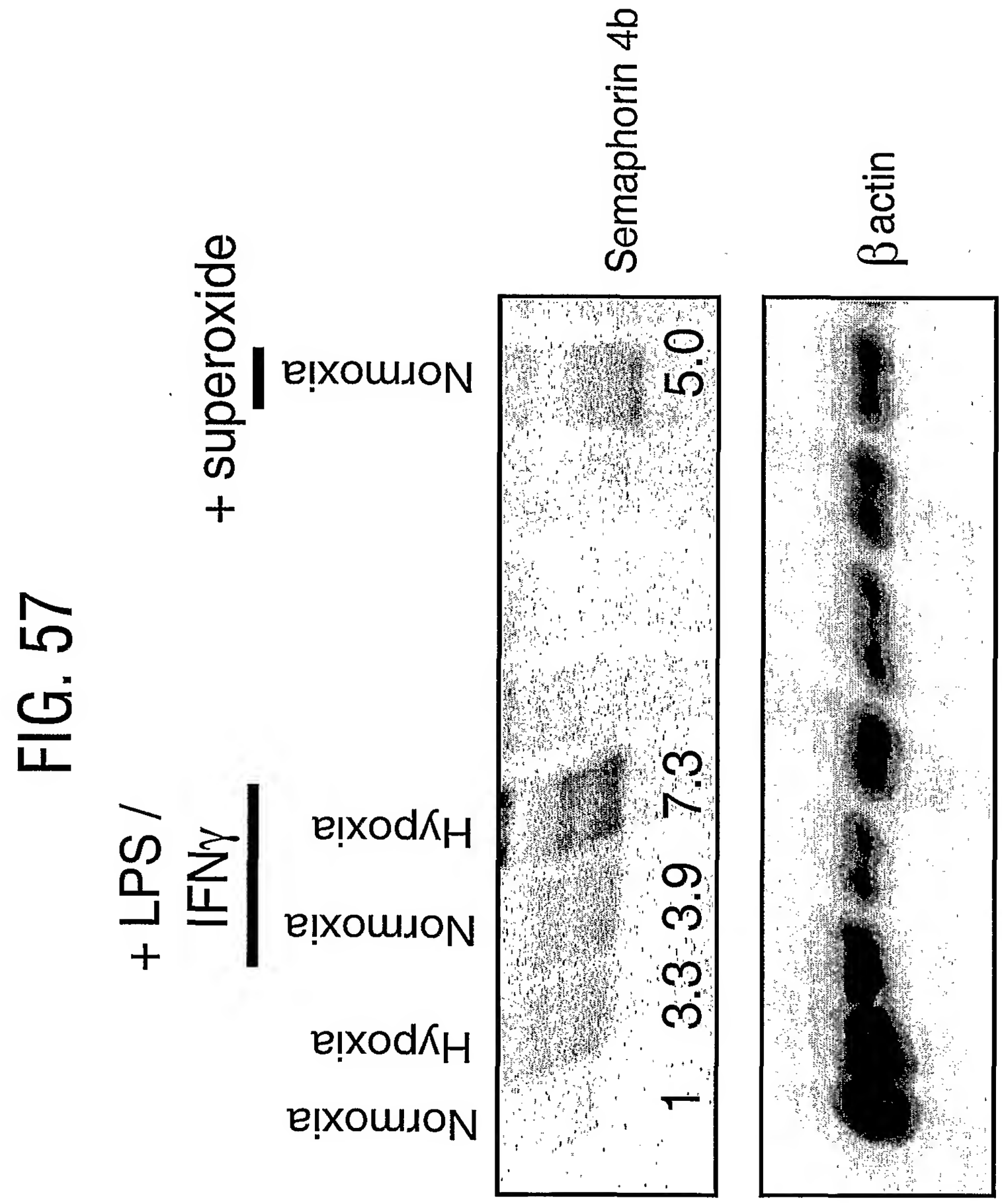
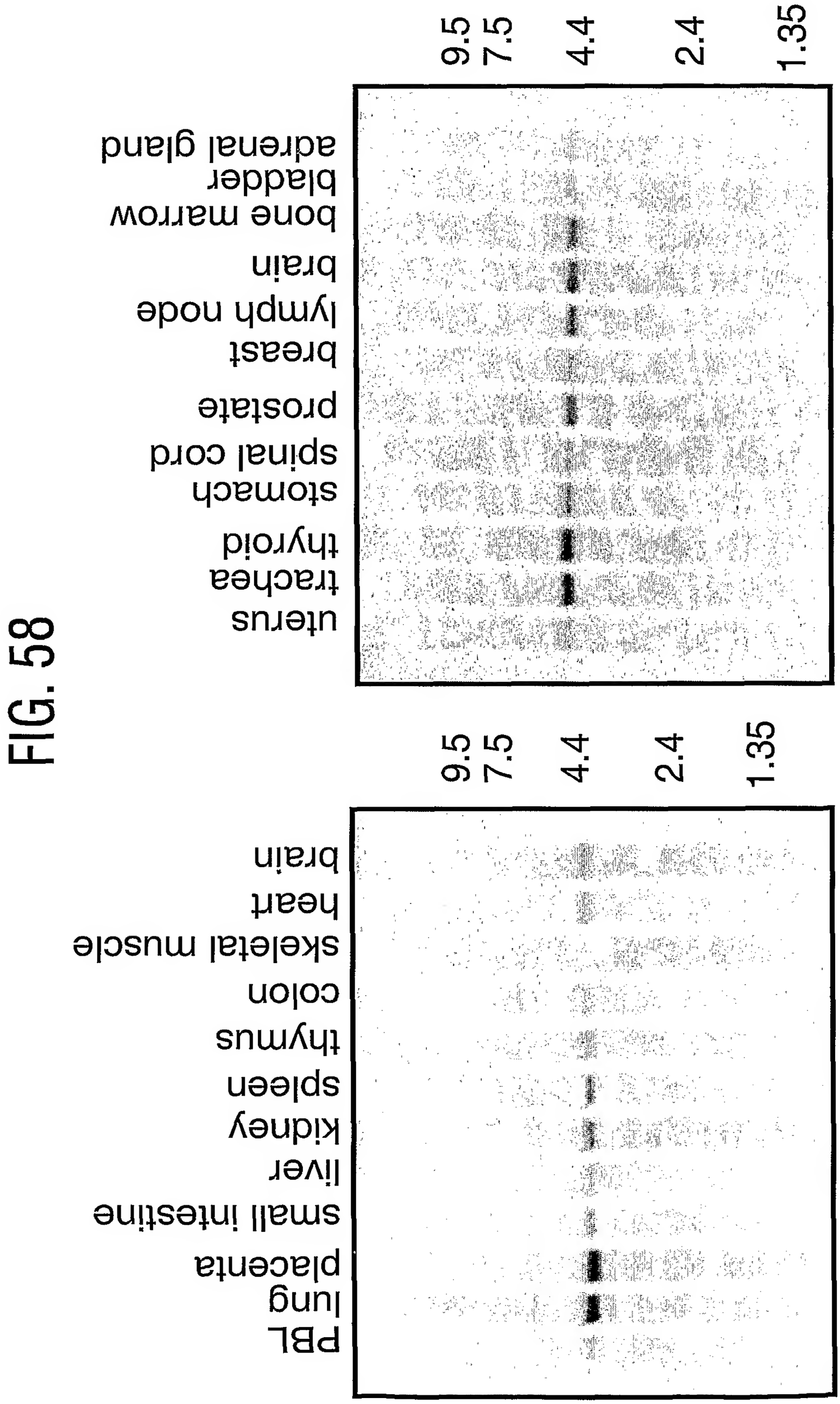

+ LPS / IFNγ
Normoxia
Hypoxia
Normoxia
Hypoxia
+ superoxide
Normoxia
1
3.3
3.9
7.3
5.0
Semaphorin 4b
βactin

FIG. 58


9.5
7.5
4.4
2.4
1.35
uterus
trachea
thyroid
stomach
spinal cord
prostate
breast
lymph node
brain
bone marrow
bladder
adrenal gland
9.5
7.5
4.4
2.4
1.35
skeletal muscle
heart
brain
colon
thymus
spleen
kidney
liver
small intestine
placenta
lung
PBL

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
13 June 2002 (13.06.2002)

PCT

(10) International Publication Number
WO 02/046465 A3

(51) International Patent Classification[7]: G01N 33/50, 33/68

(21) International Application Number: PCT/GB01/05458

(22) International Filing Date:
10 December 2001 (10.12.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

0030076.4	8 December 2000 (08.12.2000)	GB
0103156.6	8 February 2001 (08.02.2001)	GB
0125666.8	25 October 2001 (25.10.2001)	GB

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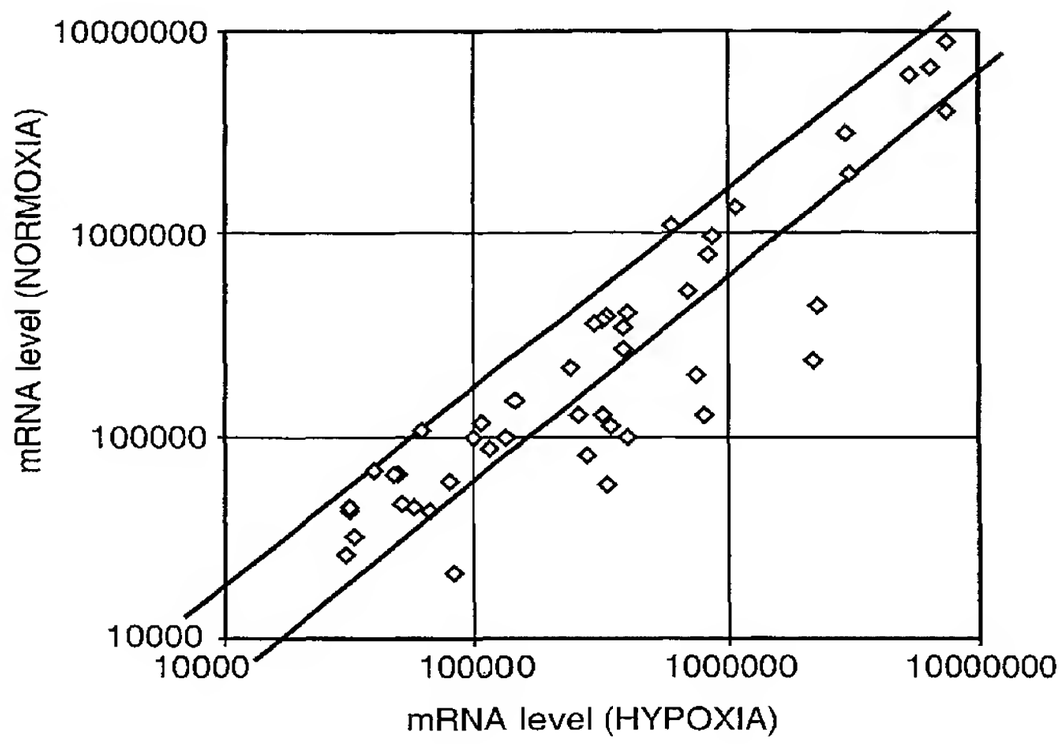
(74) Agents: **HALLYBONE, Huw, George** et al.; Carpmaels & Ransford, 43 Bloomsbury Square, London WC1A 2RA (GB).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG,

[Continued on next page]

(54) Title: METHOD FOR IDENTIFICATION OF GENES INVOLVED IN SPECIFIC DISEASES



(57) Abstract: This invention relates to novel methods for the identification of genes and gene products that are implicated in certain disease states. According to the invention, there is provided a method for the identification of a gene that is implicated in a specific disease or physiological condition, said method comprising the steps of comparing: i) the transcriptome or proteome of a first specialised cell type that is implicated in the disease or condition under first and second experimental conditions; with ii) the transcriptome or proteome of a second specialised cell type under said first and said second experimental conditions; and identifying as a gene implicated in the disease or physiological condition, a gene that is differentially regulated in the two specialised cell types under the first and second experimental conditions. The invention also relates to novel genes and gene products identified using these methods.

WO 02/046465 A3

SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

(84) **Designated States** *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

(88) Date of publication of the international search report:
6 November 2003

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 01/05458

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G01N33/50 G01N33/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 G01N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PEROU C M ET AL: "Molecular portraits of human breast tumours" NATURE, MACMILLAN JOURNALS LTD. LONDON, GB, vol. 406, no. 6797, 17 August 2000 (2000-08-17), pages 747-752, XP002203006 ISSN: 0028-0836 cited in the application	1-5,7-11
Y	page 747, right-hand column, paragraph 2 -page 749, left-hand column, paragraph 2 --- -/--	1,6

[X] Further documents are listed in the continuation of box C.

[ ] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
11 March 2003	01. 07. 2003

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Gundlach, B

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 01/05458

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; October 2000 (2000-10) TANAKA TOSHIO: "Transcriptome analysis and pharmacogenomics." Database accession no. PREV200000485122 XP002234129 abstract & FOLIA PHARMACOLOGICA JAPONICA, vol. 116, no. 4, October 2000 (2000-10), pages 241-246, ISSN: 0015-5691 ---	1,6
X	PEROU C M ET AL: "Distinctive gene expression patterns in human mammary epithelial cells and breast cancers" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 96, no. 16, 3 August 1999 (1999-08-03), pages 9212-9217, XP002203005 ISSN: 0027-8424 abstract page 9212, left-hand column, last paragraph -page 9212, right-hand column, paragraph 1 ---	1-5,7-11
A	EISEN M B ET AL: "Cluster analysis and display of genome-wide expression patterns" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 95, December 1998 (1998-12), pages 14863-14868, XP002140966 ISSN: 0027-8424 page 14863, left-hand column, paragraph 2 page 14864, left-hand column, paragraph 1 -----	1-11

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 01/05458

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: –
because they relate to subject matter not required to be searched by this Authority, namely:

see FURTHER INFORMATION sheet PCT/ISA/210

2. [X] Claims Nos.: 12, 28-31, 40, 63, 64
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [X] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-11

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claim 51 (fully) and claims 52-60 (in as far as they refer back to claim 51) are directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
Although claims 44-47 and claim 50 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box I.1

Rule 39.1(iv) PCT - Diagnostic method practised on the human or animal body
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

---

Continuation of Box I.2

Claims Nos.: 12, 28-31, 40, 63, 64

Present claims 12, 28-31, 40, 63, 64 (in full) (and the other claims in as far as they refer back to claims 12, 28-31, 40, 63, 64) relate to compounds defined by reference to a desirable characteristic or property, namely being identifiable by the screening method 61.

The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for no such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compounds by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search can only be carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the screening methods per se.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

receipt of the search report or during any Chapter II procedure.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: claims 1-11

Method for identification of genes involved in specific diseases

Inventions 2-217: claims 12-75 (all partially)

Polypeptide comprising a nucleic acid or peptide sequence according to one of SEQ ID NOs: 1-216

Invention 218: claims 76, 77

Polypeptide